A review on the removal of antibiotics by carbon nanotubes
Qiao Cong, Xing Yuan and Jiao Qu

ABSTRACT
Increasing concerns have been raised regarding the potential risks of antibiotics to human and ecological health due to their extensive use. Carbon nanotubes (CNTs) have drawn special research attention because of their unique properties and potential applications as a kind of adsorbents. This review summarizes the currently available research on the adsorption of antibiotics on CNTs, and will provide useful information for CNT application and risk assessment. Four different models, the Freundlich model (FM), Langmuir model (LM), Polanyi–Mane model (PMM), and Dubinin–Ashtakhov model (DAM), are often used to fit the adsorption isotherms. Because different mechanisms may act simultaneously, including electrostatic interactions, hydrophobic interactions, π–π bonds, and hydrogen bonds, the prediction of organic chemical adsorption on CNTs is not straightforward. Properties of CNTs, such as specific surface area, adsorption sites, and oxygen content, may influence the adsorption of antibiotics on CNTs. Adsorption heterogeneity and hysteresis are two features of antibiotic–CNT interactions. In addition, CNTs with adsorbed antibiotics may have potential risks for human health. So, further research examining how to reduce such risks is needed.

Key words | adsorption, antibiotics, carbon nanotubes

INTRODUCTION
The history of carbon nanostructures began in 1985, when the Buckminsterfullerene C_{60} was discovered by Kroto et al. (1985), and this discovery won them the Nobel Prize in 1996. Since the discovery of carbon nanotubes (CNTs) in 1991 by Iijima, CNTs have been the focus of considerable research because of their unique physicochemical properties, such as high surface area, large aspect ratio, remarkably high mechanical strength, thermal conductivity as well as electrical and optoelectronic properties. These depend on atomic arrangement (how the sheets of graphite are ‘rolled’), the diameter and length of the tubes, and the morphology, or nanostucture (Thostenson et al. 2001; Avouris 2002). CNTs can be described as graphite sheets rolled up into nanoscale-tubes (Pyrzynska 2011).

High specific surface area, abundant pore and hollow structures, and strong interactions between CNTs and pollutant molecules make CNTs potential candidates to solve environmental pollution problems. A large number of studies have already been carried out on the adsorption of small molecules (Masenelli-Varlot et al. 2002; Gaur & Shim 2008; Chen & Huang 2009), heavy metal ions (Li et al. 2002, 2003; Chen & Wang 2006), radionuclides (Chen et al. 2008b, 2009a), and organic chemicals (Goering et al. 2008b; Hyung & Kim 2008; Yang & Xing 2009) on CNTs. It was reported that various mechanisms simultaneously play roles in organic chemical adsorption, such as hydrophobic, electrostatic, hydrogen bond, and π–π interactions (Pan & Xing 2008; Ji et al. 2009). These interactions as well as hollow and layered nano-sized structures make CNTs good candidates for use as adsorbents. Their surfaces are made up of hexagonal arrays of carbon atoms in graphene sheets. These interact particularly strongly with the benzene rings of aromatic compounds. The study of the adsorption properties of CNTs plays an important role from both a fundamental and practical point of view because it could shed new light on the mechanism of adsorption in complex systems (Ren et al. 2011).

Antibiotics are widely used in human and veterinary pharmaceuticals to prevent and treat disease such as diminishing inflammation (Thiele-Bruhn 2005). A fraction of
antibiotics is unavoidably discharged into the water and soil environments mostly via domestic wastewater effluent, disposal of expired pharmaceuticals, and excretion of the original or metabolized forms (Ashton et al. 2004; Choi et al. 2008; Kemper 2008). These compounds are potentially toxic to aquatic organisms and eventually to humans through the food chain and drinking water (Maskaoui et al. 2007; Lin & Huang 2008). Even small concentrations of pharmaceuticals released from the environmental matrix into water can pose a danger to the water environment (Aga 2008). Increasing concerns have been raised regarding the potential risks of antibiotics to human and ecological health because of their extensive use (Wang et al. 2010b).

The toxic effects caused by antibiotics will be enhanced when various antibiotics are presented simultaneously. For example, growth-inhibiting effects are intensified through simple addition of binary mixtures of sulfonamides or even the synergistic effects of trimethoprim and sulfonamides (Yang et al. 2008). More importantly, antibiotic-resistant genes could be induced among microorganisms via prolonged exposure to relatively low antibiotic concentrations (Brown & Balkwill 2009), leading to the failure of antibiotics in clinical applications.

Taking into account the widespread interest in carbon nanostructures, it is not surprising that they also found some applications in the removal of antibiotics. CNTs may have significant impacts on the fate and transport of antibiotics if they are released to the environment. This review illustrates a growing number of CNT applications for the removal of antibiotics from water.

**ADSORPTION ISOTHERMS OF ANTIBIOTICS ON CNTS**

Adsorption isotherms describe how solutes interact with adsorbents. Four different models are often used to fit the adsorption isotherms. These are the Freundlich model (FM), Langmuir model (LM), Polanyi–Mane model (PMM), and Dubinin–Ashtakhov model (DAM) (Dubinin & Astakhov 1971). Table 1 summarizes the published adsorption of seven common antibiotics on different types of CNTs. Moreover, the features such as experimental conditions, adsorption capacities, adsorption equilibrium times, and the best fitting adsorption isotherm types are mentioned.

As shown in Table 1, the antibiotics can be effectively adsorbed by CNTs. The best fitting adsorption isotherm types for different antibiotics are not alike. However, the types for the same antibiotics may be different as the experimental conditions change.

**POSSIBLE ADSORPTION MECHANISMS OF ANTIBIOTICS ON CNTS**

**Electrostatic interactions**

pH may play a role in the overall adsorption process (Peng et al. 2012). Electrostatic interactions greatly control the adsorption of ionic compounds. The surfaces of all CNTs are positively charged at pH values lower than pH_{zpc} (zero point of charge) and negatively charged at pH values higher than pH_{zpc}. Some antibiotics, such as sulfamethoxazole (SMX) and norfloxacin (NOR), have two pK_{a} (acid dissociation constant) values, and can be positively charged (cationic), negatively charged (anionic), and/or zwitterionic. Therefore, electrostatic interactions between the antibiotics and the CNTs are likely one of the major factors for controlling the adsorption process. Many studies support this theory. For example, Zhang et al. (2010) reported that the adsorption coefficient (K_{d}) of SMX reached a maximum value at around pH 3.5 (see Figure 1). SMX possesses two pK_{a} values, 1.7 and 5.7 (Merck 1996; Lucida et al. 2000). The cationic, neutral, and anionic species of SMX dominated at pH < 1.7, around pH 3.7, and at pH > 5.7, respectively. The adsorption of SMX at selected pHs could provide essential information on the adsorption behavior of different SMX species. The pH_{zpc} values of hydroxylated CNTs (MH) and carboxylated CNTs (MC) are around 4. Thus, MH and MC are positively charged at pH < 4 and negatively charged at pH > 4. In the range of pH > 3.5, anionic SMX species increased with increased pH and the electrostatic repulsion between SMX and MH or MC resulted in decreased K_{d}. At pH < 3.5, apparent K_{d} decreased greatly with decreased pH because of the electrostatic repulsion between cationic SMX and positively charged MH or MC. Wang et al. (2010b) deemed that NOR has two pK_{a} values 6.2 and 8.5. The positively charged, negatively charged and zwitterionic form of NOR dominated at pH < 6.2, pH > 8.5 and pH 6.2–8.5, respectively. Taking MH for an example, at pH < 4.0 and pH > 8.5, the adsorption of NOR on MH is expected to be depressed, because NOR molecules and CNT surfaces had the same sign of charge and could repel each other. At pH between 4.0 and 6.2, the NOR molecules and CNT surfaces had opposite charges, thus the adsorption was expected to be enhanced.
Hydrophobic interactions

The hydrophobicity of antibiotics changes greatly with pH. The outer surfaces of CNTs provide evenly distributed hydrophobic sites (Pan & Xing 2008), hydrophobic interaction is another mechanism for antibiotics to adsorb on CNTs. Taking NOR as an example, at pH 7.2, NOR solubility was the lowest (Yu et al. 1994), indicating its highest hydrophobicity compared to other pHs. Wang et al. (2010b) verified that the maximum adsorption coefficient of NOR was reached at pH 7.2.

π-π electron donor–acceptor interactions (EDA mechanism)

The EDA mechanism has been considered as one of the predominant driving forces for the adsorption of chemicals with benzene rings on CNTs (Zhu et al. 2004; Gotovac et al. 2007;
Antibiotics, such as oxytetracycline (OTC), SMX and NOR, are strong π-acceptors because of their amino functional groups or fluorine group. These groups are strong electron donors, and the unshared pair of electrons of the groups can participate in strong electron conjugation with the π electrons of the electron-rich benzene rings, which can then interact strongly with polarized positively charged regions on CNTs (Chen et al. 2008a). Different surface-modified CNTs have different surface functional groups. Carboxyl groups on CNTs make MC an electron acceptor, while hydroxyl groups make MH an electron donor (Keiluweit & Kleber 2008). As proposed in the EDA theory, the interactions between a π-donor compound and a π-acceptor compound are much stronger than that between donor–donor or acceptor–acceptor pairs (Zhu et al. 2004). Therefore, the force of the EDA interactions between MC and the antibiotics decreased compared to graphitized CNTs (MG). For the same reason, the adsorption of these antibiotics on MH significantly increased relative to MG.

Hydrogen bonds

Hydrogen bonds (H-bonds) have been proposed as another mechanism for understanding adsorption of antibiotics on CNTs (Pan & Xing 2008; Pan et al. 2008). The benzene rings on the CNT surfaces may act as H-bond donors (Hickey & Passino-Reader 1991) and form H-bonds with oxygen-containing functional groups on antibiotics molecules. In addition, C = O and O–H groups on antibiotics might form H-bonds with the surface oxygen atoms of CNTs.

Multiple mechanisms, as mentioned above, act simultaneously. Different adsorption mechanisms respond to the change of environmental conditions differently. Thus, the relative contribution of an individual mechanism to the overall adsorption is of major importance to predict antibiotics adsorption on CNTs.

### ADSORPTION AFFECTED BY PROPERTIES OF CNTS

#### Specific surface area and adsorption sites

CNTs have a high specific surface area, normally in the range of 290 ± 170 m²/g, and are generally lower than that of activated carbons (ACs) (Cho et al. 2008). Wang et al. (2010b) and Carabineiro et al. (2012) reported that antibiotics adsorption on ACs is higher than that on CNTs. However, Peng et al. (2012) reported that ofloxacin (OFL) and NOR did not show the highest adsorption on ACs. Single-walled CNTs showed comparable or even higher adsorption than ACs. The high specific surface area of ACs is attributed to its porous structure (Wang et al. 2010a). It should be noted that N₂ molecules used in specific surface area measurement are much smaller than the OFL and NOR molecules. Thus, the N₂-measured ACs surface may be not completely available for OFL and NOR adsorption. However, the specific surface area of CNTs is mostly its outer exposed surface (Yang et al. 2006) and thus the availability of CNT surface would be higher than that of AC surface for OFL and NOR. Therefore, the specific surface area may not be a direct parameter to predict antibiotics–CNT interactions.

There are four possible sites (see Figure 2) in CNT bundles for the adsorption of different pollutants (Gatica et al. 2007).

![Figure 2](https://iwaponline.com/wst/article-pdf/68/8/1679/472483/1679.pdf)
et al. 2001; Agnihotri et al. 2005): inside, interstitial channels (ICs), external grooves, and outside surfaces. The adsorption reaches equilibrium much faster on external sites (grooves and outside surfaces) than on the internal sites (ICs and inside) under the same pressure and temperature conditions. The external sites are directly exposed to the adsorbing materials; the adsorption process on internal sites has to be initiated on the ends of the pore, followed by diffusion to the sites at the interior (Burd & Calbi 2007; Rawat et al. 2007). In addition, the opened CNT bundles provide more adsorption sites than capped CNTs (Ren et al. 2011).

**Oxygen content of CNTs**

CNTs can contain oxygen functional groups, such as –OH, –CO, and –COOH, which can be formed on the surfaces of CNTs depending on the synthesis procedure and purification process used. These functional groups can also be intentionally generated by oxidation using various acids (Liu et al. 1998; Toebes et al. 2004), ozone (Byl et al. 2005; Liu et al. 2006; Sham & Kim 2006), plasma (Chen et al. 2009b), or be removed by heat treatment (Takagi et al. 2007). A modification of CNTs with specific physicochemical properties can be easily achieved by chemical modification (Xie et al. 2007; Lu & Chiu 2008), such as hydroxylated (MH), carboxylated (MC), graphitized (MG) CNTs, and so on, to make them have better adsorptive capacity. The functional groups can change the wettability of CNT surfaces, making them more hydrophilic and suitable for the adsorption of relatively low molecular weight and polar compounds (Peng et al. 2003; Lu et al. 2006; Piao et al. 2008). On the other hand, addition of functional groups may increase diffusion resistance (Onyestyák et al. 2004) and decrease adsorptive surface area, which can reduce the accessibility and affinity of CNT surfaces for some organic chemicals, such as naphthalene (Cho et al. 2008) and resorcinol (Liao et al. 2008). Meanwhile, functional groups generally block the access to the interior space of the open-ended tubes.

**Adsorption Heterogeneity and Hysteresis**

Adsorption heterogeneity can be explained by two reasons. One is the presence of high energy adsorption sites, which are mainly CNT defects (Shih & Li 2008), functional groups (Fagan et al. 2004), and interstitial and groove regions between CNT bundles (Zhao et al. 2002). The other is condensation, such as surface and capillary condensation of gas or liquid adsorbates. Hysteresis presented as deviation of desorption curves from adsorption ones (Pan et al. 2008) are widely explained by the strong π-π coupling of benzene-ring containing chemicals with CNT surfaces (Wang et al. 2002), capillary condensation (Lee et al. 2006), and alteration of adsorbent structure or reorganization after adsorption (Pan & Xing 2008). Oleszczuk et al. (2009) and Wang et al. (2010a) reported that oxytetracycline (OTC) and NOR clearly showed adsorption and desorption hysteresis for CNTs.

**Potentiality of Health Risks**

Although the application of CNTs is of definite advantage in many functional areas, CNTs have detrimental impacts on health (Simate et al. 2012). Current researches have shown that CNTs are able to enter the body through the skin, respiratory tract or gastrointestinal tract, deposit themselves in several organs within the body and may cause many adverse biological effects (Hoet et al. 2004; Lam et al. 2004, 2006; Warheit et al. 2004; Oberdörster et al. 2005; Davoren et al. 2007; Li et al. 2007).

CNTs have shown multiple effects on mammalian cell systems (Upadhyayula et al. 2009). CNTs are bio-persistent and observed to induce pulmonary inflammation as well as lung cellular proliferation in rats. In another study, the materials were found to inhibit the growth of heart muscles in rats (CBC 2007). The toxicity of CNTs on mammalian cells is greater than quartz (Dreher 2004; Jia et al. 2005) and asbestos (Wick et al. 2007). Furthermore, there are concerns that CNTs may interfere or damage DNA, and could have harmful effects on organs if introduced into the body (Kolosniaj et al. 2007). At present, only a few studies on the genotoxicity of CNTs have been published. Patiolla et al. (2010) investigated the toxicity of purified CNTs in normal human dermal fibroblast cells using cell viability, DNA damage and apoptosis as the toxicological endpoints. The results clearly indicated a significant increase in cytotoxicity, genotoxicity and apoptosis in the normal human dermal fibroblast cell line, due to exposure to CNTs. Zhu et al. (2007) found that CNTs can accumulate and induce apoptosis in mouse embryonic stem cells and activate the tumor suppressor proteins. The CNTs which were predominantly single-walled were found to be genotoxic in the human bronchial epithelial cell line, exhibiting an epithelial phenotype, as measured by the alkaline comet assay and the micronucleus assay (Lindberg et al. 2009). In addition, the toxicity will also depend on whether they are persistent or
cleared from the different organs of entry, and whether the host can generate an effective response to sequester or dispose of the particles (Card et al. 2008).

CNTs with adsorbed antibiotics may exhibit the toxicity once they are in contact with living organisms (Wang et al. 2010b). CNTs may be functionalized by antibiotics, and functionalized CNTs can cross cellular barriers by altering their interaction with cells and alteration of intracellular transport kinetics of the functionalized CNTs (Jain et al. 2012). Therefore, it is important to consider the coexistence of CNTs and antibiotics. However, at the present there are no well-defined global agreements about the risks of CNTs on human health (Stella 2011).

CONCLUSIONS

This review presents the applications of CNTs for the adsorption of antibiotics. CNTs have a strong adsorption affinity. CNTs provide a large specific surface area and a strong van der Waals binding energy for molecular adsorbates on well-defined adsorption sites such as inside, interstitial channels, external grooves, and outside surfaces. According to experimental and theoretical research, electrostatic interactions, hydrophobic interactions, π–π electron donor–acceptor interactions and hydrogen bonds may be possible mechanisms of antibiotics adsorption on CNTs. Various mechanisms may simultaneously control antibiotics adsorption on CNTs. Each adsorption mechanism may be affected differently by environmental conditions. Therefore, it is of great importance to obtain the relative contribution of different mechanisms to the overall adsorption in the future.

Wider applications of CNTs have been facilitated by the improvement in their productions. In all carbon nanomaterials, cost has been a main limiting factor of commercialization. However, it is widely believed that if production volumes increase, costs would decrease markedly. Moreover, in spite of high costs, using CNTs as adsorbents may be advantageous in future because the high adsorption capacities of CNTs compared to other media may offset their high cost. In addition, many researchers are branching out with the modification of CNTs by innovative processing techniques. However, there is still a lot of work to enhance CNT adsorption properties in future.

From the other side, there has been great concern about whether CNTs are toxic and could enter the environment as suspended particulate matter of respirable sizes. Results presented today showed that CNTs may have potential risks for health. So, further research examining how to reduce the risks is needed. A better understanding of antibiotic–CNT interaction mechanisms and subsequent environmental behavior of both antibiotics and CNTs will provide a fundamental basis for the prediction of CNT risks. In addition, being aware of CNT risks would help to develop related guidelines for safe design and application of CNTs.

ACKNOWLEDGEMENT

The authors would like to acknowledge the financial support of the National Natural Science Foundation of China (51309013).

REFERENCES


