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# Adsorption of uraemic toxins on carbon nanotubes

Chao Ye [a,*], Qian-Ming Gong [a], Fang-Ping Lu [b], Ji Liang [a]

[a] *Department of Mechanical Engineering, Tsinghua University, Beijing 100084, People's Republic of China*
[b] *Department of Nephrology, The First Affiliated Hospital of Tsinghua University, Beijing 100016, People's Republic of China*

**Abstract**

The adsorption properties of two representative uraemic toxins (i.e., creatinine and vitamin $B_{12}$) on CNTs were studied compared with two commercial haemoadsorbents (i.e., activated carbon and macroporous resin). Results show that it takes only 15 and 10 min for CR and $VB_{12}$ to achieve the adsorption equilibrium on CNTs. The adsorption amount of $VB_{12}$ on CNTs reaches 47.18 mg/g, which is 5.5 and 10.8 times of that of macroporous resin and activated carbon, respectively. Pore structure analyses indicate that the high adsorption efficiency should be attributed to the higher ratio of mesopores and macropores and the higher pore volume of CNTs. All of the results imply the great potential applications of CNTs in haemoperfusion.


*Keywords:* Carbon nanotube; Adsorption; Middle molecular weight toxin; Haemoperfusion

## 1. Introduction

Approximately one million patients throughout the world undergo chronic renal failure [1]. Uraemic toxins may accumulate to a high level in the blood of renal failure patients. Haemodialysis (HD) permits the removal of excess fluid, ions and water soluble low molecular weight toxins (MW < 500 Da), but prohibits the removal of middle molecules (MMS, term coined by Bapp et al. [2]) which are believed to be associated with the high mortality and long-term complications (e.g. amyloidosis, cardiovascular disease and microinflammation) of haemodialysis [3]. Recently, high flux haemodialysis and haemofiltration have been utilized to remove middle molecules. However, in those processes, nonspecific adsorption of middle molecules on the high flux membranes and the filter materials is generally believed to account for the large proportion of the clearance [4,5]. On the other hand, the pioneering work of Yatzidis and Chang, haemoperfusion, i.e., the direct contact of the patients' blood with sorbents, has shown higher efficiency of the removal of middle molecules [6–8]. Furthermore, adsorption can remove toxins without introducing any other substances into the blood [9]. Therefore, haemoperfusion might have more advantages over other therapies in the removal of middle molecule uraemic toxins.

All sorbents used in blood system must meet strict standards concerning biocompatibility, mechanical strength and size, etc. But the adsorption capability is still a crucial factor, which determines the efficiency of haemoperfusion. At the same time, a higher adsorption rate can alleviate the patients' pain during the therapy [10], which is also of great importance in clinic. Sorbents used currently in haemoperfusion mainly include activated carbon and polymeric resin [1]. Literatures suggest that polymeric sorbents (e.g., cross-linked styrene divinylbenzene resin) with a hydrophobic surface are associated with significant bio-incompatible symptoms, such as complement activation, neutropenia and thrombocytopenia. Such problems can be resolved to some extent by coating with haemocompatible materials, while coating would damnify the adsorption of middle molecules inevitably [3]. Recently, much attention has been paid to activated carbon derived from synthetic polymers. Since carbon materials have chemically inert surface and excellent biocompatibility, they are more powerful sorbents than their inorganic or organic counterparts because they do not require special coatings [11]. Yang et al. prepared activated carbon spheres from phenolic–resin blended with ferrocene. The adsorption of vitamin $B_{12}$ (MW = 1355 Da) on the production achieved equilibrium at approximate 210 min with the adsorption amount of 8 mg/g [12]. Malik et al. prepared activated

* Corresponding author. Tel.: +86 10 62773641; fax: +86 10 62782413.
*E-mail address:* yechao99@mails.tsinghua.edu.cn (C. Ye).

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carbon spheres by carbonizing and then activating of commercial macroporous resins (MN500HS, XAD4HS and CT275). The adsorption of IL-1β (MW = 17400 Da) achieved equilibrium in 2 h and the amount reached 0.15 μg/g [3]. Research works of both groups indicated that the highly developed mesopores are the key factor for the removal of middle molecules.

Carbon nanotubes (CNTs), with nano-sized diameter and tubular microstructure, have been the worldwide hotspot of study since their discovery due to their unique morphologies and various potential applications [13–16]. Because of their relatively large specific surface areas and easily modified surfaces, CNTs have attracted researchers' interests as a new type of sorbent [17]. Li et al. found that CNTs were better than conventional sorbents in removing of $Pb^{2+}$, $Cd^{2+}$, $F^-$ and 1,2-dichlorobenzene from water. In particular, the adsorption of those adsorbates on CNTs can achieve equilibrium only in 30 min, indicating that the adsorption rates were very fast [18–21]. In addition, nitrogen adsorption tests showed that CNTs possess highly developed mesopores in the form of "aggregated pores" [22]. Therefore, CNTs might be ideal sorbents for the removal of middle molecular uraemic toxins.

In this study, creatinine (CR, MW113 Da) and vitamin $B_{12}$ ($VB_{12}$, MW1355 Da) were chosen as the representatives of low molecular weight toxins and middle molecular toxins, respectively, to investigate the adsorption capability and rate of CNTs in haemoperfusion, complying with the Chinese industrial standard YY0406-2003 (i.e., single use haemoperfutor). At the same time, two commercial haemoadsorbents were introduced as contrast.

## 2. Materials and method

### 2.1. Materials

CNTs were prepared by pyrolysis of propylene ($C_3H_6$) with Ni as the catalyst at 750 °C. Then the as-produced CNTs were treated with $HNO_3$ solution (30%, v/v) for 24 h to remove the remnants of catalyst. Two typical commercial haemoadsorbents, i.e., activated carbon, the sorbent of the haemoperfusor TS-150 and macroporous styrene divinylbenzene resin, the sorbent of the haemoperfusor ZX-150, were adopted in contrast to CNTs (Note: both of the two haemoperfusors were produced by Aier haemopurifor factory, PR China). creatinine and vitamin $B_{12}$, reagent grade, were obtained from Beijing Chemical Reagent Company.

### 2.2. Characterization

The specific surface areas and pore structure parameters of CNTs and the contrastive materials were calculated from the adsorption isotherms of nitrogen at 77 K with a SORPTOMATIC 1990 surface area analyser. The BET equation and BJH method were used to calculate the specific surface area and the pore distribution, respectively. Particle size distribution of CNTs was obtained by laser light scattering with a Malvern Mastersizer 2000 analyser. Microstructures of CNTs were observed by transmission electron microscopy (TEM) (JEOL JEM-200CX, 200kv) and high-resolution transmission electron microscopy (HRTEM) (JEOL JEM 2010F, 200 kV).

### 2.3. Adsorption of uraemic toxins

CR and $VB_{12}$ solutions were prepared by dissolving the reagents in deionized water. Adsorption isotherms were obtained by the experiments of adding 0.05 g CNTs into 100 ml solutions of CR and $VB_{12}$ with initial concentrations from 10 to 100 mg/L. After shaken for 120 min at 37 °C with a SHA-B shaker, the suspensions were filtered through the 0.45-μm membrane filters. The filtrates were analyzed by a UV-9100 spectrophotometer and the adsorption amounts were calculated as follows:

$$q = (C_0 - C_t)\frac{V}{m} \quad (1)$$

where $q$ is the adsorption amount (mg/g), $C_0$ the initial concentration (mg/L), $C_t$ the concentration after shaking process (mg/L), $V$ the volume of the solution (L) and $m$ is the dosage of CNTs (g). Correspondingly, the adsorption rate was measured by adding 1 g CNTs into 2000 ml solution with the initial concentration of 100 mg/L. As contrast, the adsorption isotherms and rates of CR and $VB_{12}$ on activated carbon and macroporous resin were studied in the same way.

## 3. Results and discussion

Fig. 1 illustrates the adsorption isotherms of CR on CNTs, macroporous resin and activated carbon, representing the adsorption capacities of the three sorbents. The adsorption capability of CNTs is a little less than that of activated carbon, but much higher than that of macroporous resin. Fig. 2 shows the adsorption isotherms of $VB_{12}$ on the three sorbents. CNTs have much higher adsorption capability of $VB_{12}$ than macroporous resin and activated carbon. The adsorption amount of $VB_{12}$ on CNTs is 47.18 mg/g at the initial concentration of 100 mg/L, which is 5.5 and 10.8 times of that of macroporous resin and activated carbon, respectively. Generally, CNTs have great advantages in the adsorption of MMS besides their high adsorption capability of low molecular toxins.

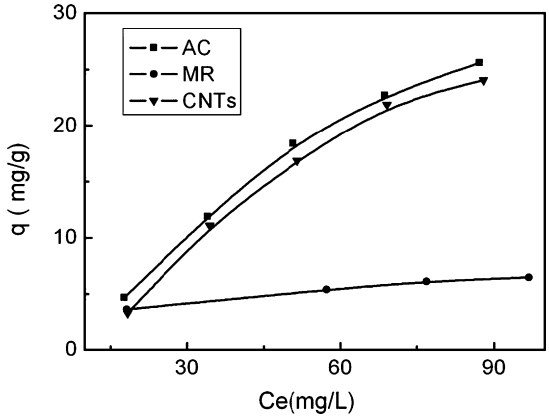


Fig. 1. Adsorption isotherms of CR for the three sorbents.

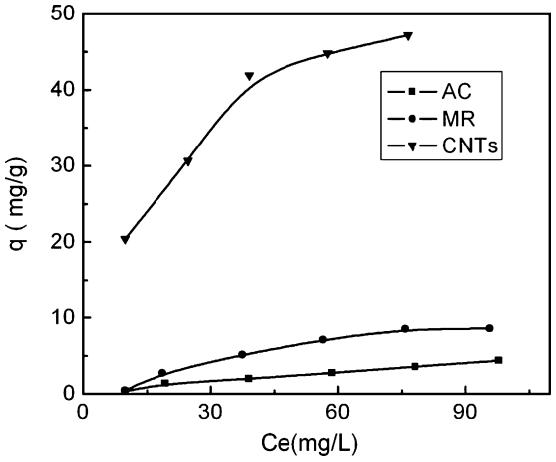


Fig. 2. Adsorption isotherms of $VB_{12}$ for the three sorbents.

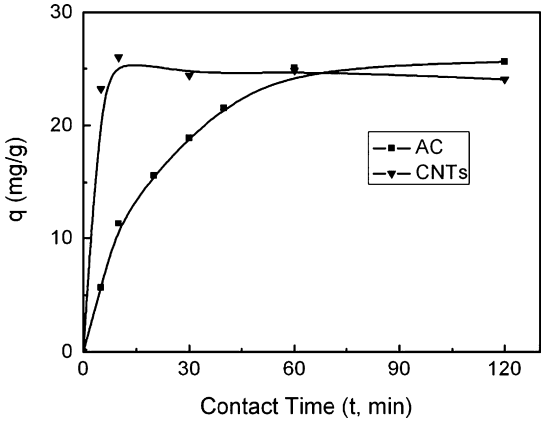


Fig. 3. Adsorption rates of CR on AC and CNTs.

Adsorption kinetics, indicating the adsorption rate, is another important character for sorbents [21]. Higher adsorption rate means shorter adsorption time and more significantly, implies alleviating the patients' pain during clinical haemoperfusion. Usually the time span of clinic haemoperfusion is approximate 120 min. Therefore, adsorption rate in 120 min is of great importance. Figs. 3 and 4 show the adsorption rates of CR and $VB_{12}$ on CNTs, respectively. Since activated carbon is much more effective than macroporous resin in removing CR, the comparison of the adsorption rate of CR between CNTs and activated carbon is more reasonable than that between CNTs and macroporous resin. The similar reason for the comparison of the adsorption rate of $VB_{12}$ between CNTs and macroporous resin is shown in Fig. 4. The adsorption rates of CR and $VB_{12}$ on CNTs are rather high at the initial stage. The adsorption processes achieve equilibrium quickly at about 15 min and 10 min, while the time for the adsorption equilibrium of CR on activated carbon is about 60 min and the time for that of $VB_{12}$ on macroporous resin is 120 min. The results indicate that CNTs would be more applicable as sorbents in haemoperfusion than activated carbon and macroporous resin, although much work leaves to be done before CNTs applied in clinical.

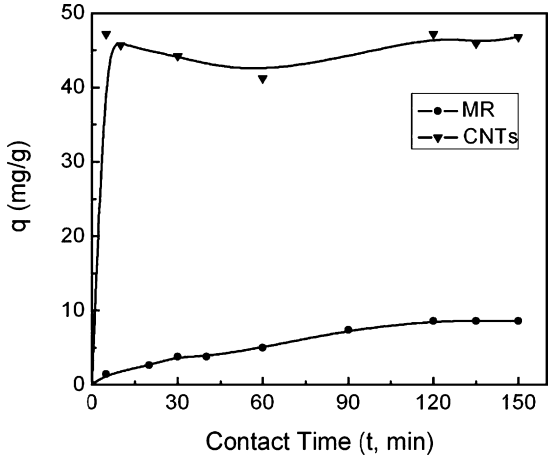


Fig. 4. Adsorption rates of $VB_{12}$ on MR and CNTs.

TEM and HRTEM images of CNTs are shown in Fig. 5. The outer diameters and inner cavities of those tubes are approximate in the range of 20–50 nm and 8–15 nm, respectively. Fig. 6 exhibits the pore size distributions of the three sorbents. The specific areas and pore volume parameters of the three sorbents are listed in Table 1. According to International Union of Pure and Applied Chemistry (IUPAC), pores can be classified as follows: (1) micropores (width less than 2 nm), (2) mesopores (width

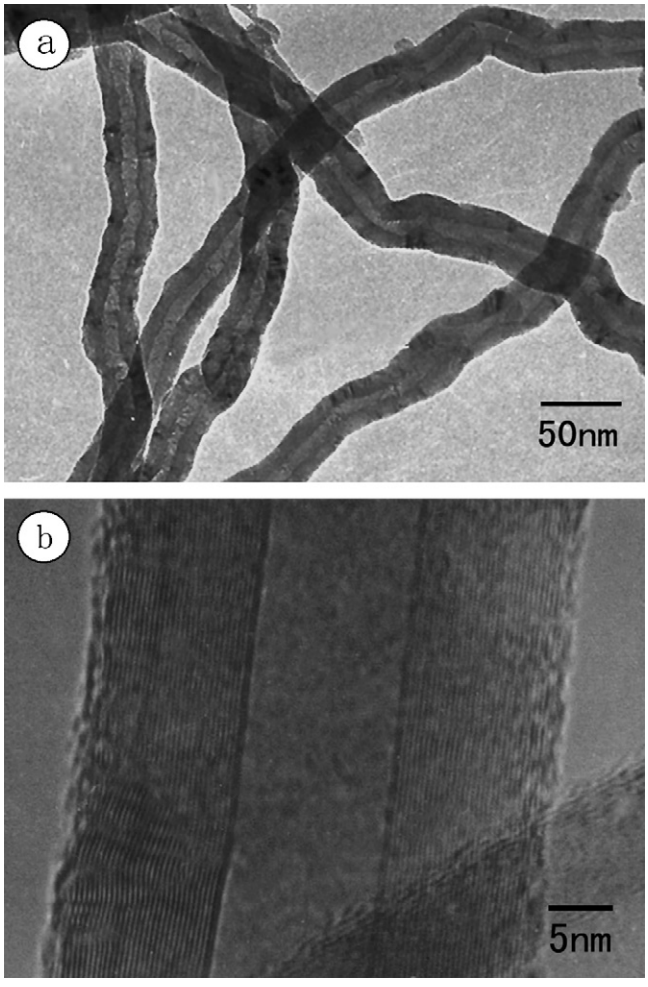


Fig. 5. TEM and HRTEM images of CNTs: (a) TEM image and (b) HRTEM image.

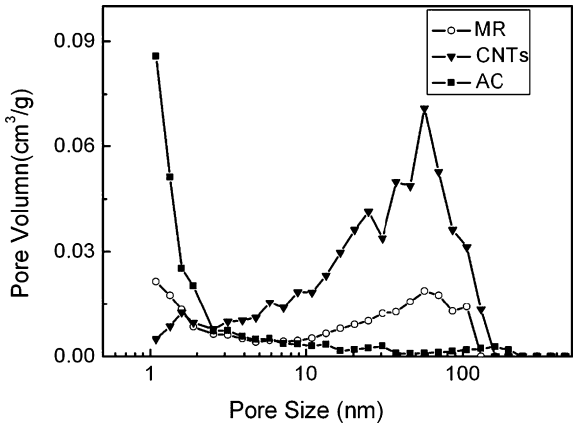


Fig. 6. Pore size distributions of the three sorbents.

between 2 and 50 nm) and (3) macropores (width greater than 50 nm) [1].

CNTs contain mesopores and macropores chiefly. Only 5.8% of the pore volume is contributed by micropores. These micropores may be constructed by the opened inner cavities with very small diameters and defects on graphite lattice. The volumes of mesopores and macropores of CNTs are 0.439 and 0.134 $cm^3/g$, which are 72.2% and 22.0% of the total pore volume, respectively. These pores are mainly provided by the opened inner cavities and the so-called "aggregated pores" [22]. The pores larger than 20 nm contribute 68.1% of the total pore volume. These pores might be associated with the aggregated pores, since the inner cavities of CNTs are less than 20 nm in most cases. Macroporous resin shows obviously bimodal pore distribution (micropores and macropores). However, micropores account for 77.4% of the total pore volume of activated carbon. As a result, the pore volume of CNTs is the largest among the three sorbents although CNTs possess the lowest specific surface area.

The first prerequisite of adsorption is that the molecules of the adsorbate are smaller than the pore size so that they can diffuse through the entrance into the inner part of the pores. Another prerequisite is that the molecules of the adsorbate and the pore walls could interact physically or chemically. CR is a small molecule with a molecular size of 0.54 nm, which is in the range of micropore. Therefore the adsorption capability depends on the quantity of the active sites on which CR molecules are adsorbed [12]. Both CNTs prepared by CVD method and activated carbons have many defects on graphite lattice. Carbon atoms around the site of crystal defects often have higher free energy than those in regular graphite lattice since they contain dangling C–C bonds. Thus the sites with crystal defects are more reactive so that the adsorption of small molecules can be more easily achieved. It has been approved by infrared ray (IR) spectra analyses that the adsorption of several function groups (e.g., carboxylic acid groups and carbonyl groups) on CNTs is extremely associated with the defects on graphite lattice [23]. However macroporous resin is a type of stable polymeric compound with saturated bonds so that it has few activated sites. Consequently, the adsorption capability of CR on CNTs is similar to that of activated carbon but much higher than that of macroporous resin.

Table 1
Pore volumes and BET specific surface areas of the three sorbents

| | CNTs | AC | MR |
|---|---|---|---|
| Micropore volume ($cm^3/g$) | 0.0357 | 0.224 | 0.0754 |
| Mesopore volume ($cm^3/g$) | 0.439 | 0.0553 | 0.133 |
| Macropore volume ($cm^3/g$) | 0.134 | 0.0114 | 0.0446 |
| Total pore volume ($cm^3/g$) | 0.608 | 0.290 | 0.253 |
| BET surface area ($m^2/g$) | 122 | 1042 | 600 |

However, $VB_{12}$ is a typical MMS with a molecular size of 2.09 nm. Therefore, $VB_{12}$ molecules can only enter into the mesopores and macropores larger than 2.09 nm. Pores in activated carbon are mostly smaller than 2 nm, thus the adsorption capability of $VB_{12}$ on activated carbon is quite limited. Once the pore walls have been occupied by $VB_{12}$ molecules, the pore diameters would be reduced, which hinders the further entrance of $VB_{12}$ [12]. Therefore, to ensure large adsorption capabilities, large pore diameters and volumes are needed. CNTs have the largest pore diameters and volumes so that the adsorption capability of $VB_{12}$ on CNTs is much higher than that of the other two counterparts.

The adsorption process can be described as the following two steps. First the molecules of adsorbate diffuse into the pores of the sorbents from the solution. Second, the molecules are adsorbed by the pore walls. Since the latter process can be finished rapidly, the adsorption rate is determined by the rate of the diffusion. As shown in Fig. 7, the particle sizes of CNTs are mainly less than 100 μm. However, both of activated carbon and macroporous resin have the particle sizes of 6–12 mm, which are much larger than that of CNTs. So the diffusion distances of the molecules of adsorbate in CNTs are much shorter than that in the bulky activated carbon and macroporous resin. Thus it is much faster for the molecules of CR and $VB_{12}$ to diffuse into the pores of CNTs than into the pores of the other two sorbents. On the other hand, the pore diameters of CNTs are larger than that of activated carbon and macroporous resin, which is also beneficial to the diffusion of the molecules of CR and $VB_{12}$ into the inner part of CNTs.

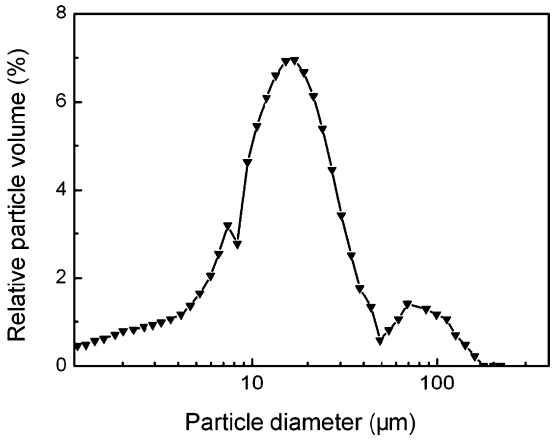


Fig. 7. Particle size description of CNTs.

## 4. Conclusion

Creatinine and vitamin $B_{12}$ were employed as the representatives of low and middle molecular weight uraemic toxins, respectively. Depending on their large pore diameters and volumes, CNTs have large adsorption capabilities for both of the two substances, especially for MMS. The adsorption amount of vitamin $B_{12}$ on CNTs from the solution with the initial concentration of 100 mg/L is 5.5 and 10.8 times of that of the two contrastive haemoperfusion sorbents, i.e., macroporous resin and activated carbon. The adsorption rates are also much faster on CNTs, which is attributed to their smaller particle sizes, larger pore diameters and pore volumes. CNTs are proved to be a better alternative to the current sorbents and show great potential applications as the sorbent of haemoperfusion.

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