Immobilization of highly-dispersed single-walled carbon nanotubes in biocompatible and water-soluble solid matrix

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Purified HiPco SWNTs were dispersed in lactose aqueous solutions containing sodium deoxycholate (SDC) as the dispersant, with the assistance of ultrasonication. After removing the large bundles of SWNT by high speed centrifugation, the resulted SWNTs aqueous dispersion was spray-dried, and then the SWNTs-lactose solid dispersions (or composite particles) were obtained. They were mostly of spherically shell-structured shape with several microns in diameter. Vis-NIR spectroscopy and TEM observation revealed that SWNTs presented as small bundles and individual tubes inside the lactose solid matrix. These results indicated that lactose precipitated out from the aqueous droplets in the spray-drying, and transformed to solid matrix rapidly, which prevented the dispersed SWNTs from re-aggregation, thus immobilize the isolated SWNTs inside the matrix. The present solid dispersions can readily be re-dispersed in water and form SWNTs aqueous dispersion.

Key-words : Single-walled carbon nanotubes, Spray-dry, Solid dispersion, Lactose, Sodium deoxycholate

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1. Introduction

Due to the nanoscale dimensions and outstanding materials properties, single-walled carbon nanotubes (SWNTs) received extensive attention since its discovery. SWNTs obtained from various methods are mixtures of tubes with different length and diameter, and several hundreds of single tubes aggregate together to form bundles or ropes through strong van der Waals attraction. The aggregation was found to be a severe obstacle to most potential applications of SWNTs. For decades, several approaches, including surfactant encapsulation, polymer wrapping, and chemical modification, were suggested to dissolve individual tubes or small bundles of SWNTs in organic or aqueous media.1-7 The demands of recent Nano Risk evaluation8,9 also urged researchers to obtain SWNTs dispersions for in vitro/in vivo toxicity and safety tests. The SWNTs dispersions should contain mainly single tubes or small bundles in biocompatible aqueous medium, which are suitable for inhalation/spray administration to animals.10 As the water-based carbon nanotube dispersions may sediment over time,11 long-term stability of the SWNTs dispersions is also very important.

In this study, we firstly utilized the concept of solid dispersion to “freeze” or “immobilize” the highly dispersed SWNTs (individual tubes or small bundles) in biocompatible and water-soluble particulate solid matrix. The solid dispersion, which was defined as a dispersion of one or more active ingredients in solid matrix, was a widely used pharmaceutical technology.12,13 For Nano Risk evaluation, such solid dispersions can be used directly as SWNTs delivery system, or as aqueous solution of various SWNTs concentration soon after re-dispersed in water. Here, we reported a simple spray drying technique to immobilize the highly dispersed SWNTs in a solid matrix composed of lactose and a dispersant. Sodium deoxycholate (SDC), an anionic surfactant, was selected as the dispersant of SWNTs according to our previous results.14 Both lactose and SDC are widely used pharmaceutical excipients with good biocompatibility, and indexed in many pharmacopoeias.

2. Experimental

2.1 Materials

Purified SWNTs (Lot: SP0330) produced by HiPco method was obtained from Carbon Nanotechnologies INC, USA. Sodium deoxycholate (SDC) was purchased from Sigma-Aldrich Inc, Germany. Monohydrated lactose and ethanol (> 99.5%) were obtained from Chameleon Reagent, Osaka, Japan.

2.2 Preparation of SWNTs-lactose solid dispersions

The formation procedure of the SWNTs solid dispersion was shown in Fig. 1. A modified ultrasonication method with the aid of ceramic balls12 was used for the preparation of SWNTs aqueous dispersions. Typically, 0.3 g SWNTs and a certain amount of zirconia balls (3 mm in diameter) were placed into glass bottles, and then the aqueous solution of SDC and lactose was added. The concentrations of SDC and lactose were 3.5% w/v and 10% w/v, respectively. The mixture was ultrasonically treated using a bath-type sonicator (VS-02RD Ultrasound Cleaner, Japan) for 24 h. The resulted suspensions were then centrifuged with High Speed Refrigerated Micro Centrifuge (MX-301, TOMY) at 8,000 r/min, 20°C for 1 h. The supernatants were carefully decanted and
spray-dried using B–191 Mini Spray Dryer (Büchi Labortechnik AG, Switzerland). The inlet temperature was set to 140°C, the air flow rate was 600 l/h, the feed rate was 3 ml/min, and the outlet temperature was about 90°C. After the spray-drying of the droplets, lactose precipitated out, resulting in spherical SWNTs-lactose solid dispersions.

2.3 Characterization
Size and morphology of the spray-dried SWNTs-lactose solid dispersions were examined using SEM (Era8800FE SEM, Elionix, Japan). The dispersing state of SWNTs was observed by TEM. For SWNTs dispersion in aqueous medium, one drop of liquid dispersion samples was deposited onto carbon coated TEM grid, rinsed carefully with deionized water, dried, then observed on a JEM–1010 TEM equipment (JEOL). The particulate solid dispersion was mixed with epoxy resin, after curing, the bulk solid was cut into thin slices of 70 nm thickness with a microtome device (2088 Ultrotome V, LKB, Sweden), and observed on a JEM–2000FX TEM (JEOL). The vis-NIR spectroscopy was performed to verify the dispersing states of SWNTs in solutions and particulate materials. The vis-NIR spectroscopic measurements were performed on a UV–3100PC UV-vis-NIR spectrophotometer (Shimadzu, Japan) with wavelength of 400–1100 nm. The spectra of solution samples were obtained using quartz cells. For the dry powder samples, the diffuse reflectance spectroscopy (DRS) was performed using an integrating sphere attachment (ISR–2200, Shimadzu).

3. Results and discussion
Figure 2(a) and (b) show the SEM image of as-received HiPco SWNTs and the photograph of the mixture of SWNTs and water (b) and SWNTs dispersion in aqueous solution of SDC and lactose (after centrifugation) (c).

Figure 3 showed the SEM image of the solid dispersion obtained by spray drying of the supernatant SWNTs solution (solution after centrifugation). They were of spherical shape of several microns in diameter, composed mainly of SWNTs and lactose. The lactose matrix includes free SDC (non-adsorbed on...
Further analysis revealed that they were hollow particles with the shell thickness of about 1 μm or less. We also found that non-spherical particles were obtained when only SDC was used. The effect of the lactose on the formation of spherical solid particles during spray-drying will be discussed in a separate paper. The interesting feature of the prepared solid dispersions is that they can readily be dissolved in water without any sonically treatment, resulting in the same dispersing state as shown in Fig. 2(c).

Figure 4 showed the TEM images of samples prepared from the supernatant SWNTs solution and the solid dispersion. As shown in Fig. 4(a), after the ultrasonically treatment, the SWNTs were finely dispersed, compared with the as-received state (Fig. 1(a)). The SWNTs in the supernatant were mainly small bundles and might include individual tubes with length less than 1 μm. The TEM image in Fig. 4(b) provided a direct indication to the dispersion state of SWNTs in the solid dispersion. It was obvious that the carbon tubes presented mainly as small bundles inside the lactose solid matrix.

Figure 5 showed a set of vis-NIR spectra of solution samples (a) and solid powder samples (b). Sharp absorbance peaks were observed for the supernatant SWNTs solution, reconstituted solution from the SWNTs-lactose solid dispersions and the SWNTs-lactose solid dispersions. For comparison, the spectrum of the physical mixture of as-received SWNTs, SDC and lactose was also recorded, which gave no sharp absorption peaks. Theory predicts that quasi one-dimensionality of SWNTs causes the electronic density of states to have a series of sharp van Hove maxima at energies dependent mainly on tube diameter. The broaden absorbance peaks and red-shifted features mean that carbon nanotubes aggregated into larger bundles. The well-resolved absorbance peaks observed were good indicators of the presence of single tubes and small bundles in the supernatant SWNTs solution, the reconstituted solution and the SWNTs-lactose solid dispersion.

Chatterjee et al.16) described the preparation of SWNTs dispersions in water-soluble polyethylene oxide by surfactant-assisted dispersion in aqueous polymer solution, followed by convective flow and vacuum drying process. In their investigation, broadening of the von Hove transition in the dried polymer-SWNTs films was observed, which was due to the re-aggregation of some of the tubes during the drying process. The sharp von Hove maximum in the spectrum of SWNTs solid dispersions in Fig. 5(b) indicated the highly dispersed state of carbon nanotubes in the solid matrix, which was in accordance with the TEM observation.

As a good dispersant of SWNTs, SDC can effectively intercalate SWNTs bundles and encapsulate the carbon nanotubes.5)14) With the evaporation of water from the aqueous dispersion, lactose precipitated out and transformed to solid matrix, which prevented the dispersed carbon tubes from re-aggregation, thus "freeze" the carbon tubes inside the solid matrix. The hydro-

![Fig. 4. TEM images of samples prepared from the supernatant SWNTs solution (a) and the SWNTs-lactose solid dispersion (b).](image)

![Fig. 5. Vis-NIR spectra of SWNTs dispersions and physical mixture. (a) Solution samples: The supernatant SWNTs solution and the reconstituted SWNTs solution from the SWNTs-lactose solid dispersion. (b) Powder samples: SWNTs-lactose solid dispersions and the physical mixture of as-received SWNTs, SDC and lactose powders.](image)
philic nature of lactose and SDC also made the solid dispersion readily re-dissolvable in water. The vis-NIR spectrum (Fig. 5(a)) also showed that after re-dissolving the solid dispersion in water, the dispersing state of SWNTs could be recovered, and no significant re-aggregation of carbon nanotubes occurred.

The prepared SWNTs-SDC-lactose solid dispersion could be used as the working sample for carbon nanotubes risk evaluation. For inhalation/spray administration, the particulate solid dispersions can be applied directly, or after re-dispersed in water to form SWNTs solution of various concentrations as needed. The quantitative vis-NIR analysis procedure for the determination of SWNTs concentration in the solid matrix was established, and in the present case, the SWNTs concentration estimated was about 1% w/v.

As well known, the poor dispersibility of SWNTs had greatly hindered its wide applications, especially as enhancing fiber in the polymer composite materials. The present results indicated a possibility to obtain pellets containing highly dispersed SWNTs, which may find applications in the fabrication of master batch material for manufacturing of SWNTs enhanced composite materials.

4. Conclusion

In this study, spray-drying method was firstly applied to prepare biocompatible SWNTs solid dispersions. The vis-NIR spectrum and TEM image of the solid samples gave a direct indication that the carbon tubes were highly dispersed inside the solid matrix mainly as small bundles and individual tubes after spray-drying. Such solid dispersions can be applicable for Nano Risk evaluation. The spray-drying method may become a promising way for large scale manufacturing of highly dispersed SWNTs hybrid materials with polymeric or inorganic materials.

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