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# Synthesis of mesoporous carbon spheres and release of albendazole

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ABSTRACT

A facile stirring method was developed to synthesize mesoporous carbon spheres (MCS), which were then loaded with the poorly water-soluble drug, albendazole (ABZ), to enhance its solubility and dissolution kinetics. The effects of the mass ratio of glucose/silica on the physicochemical properties of the resulting MCS were investigated. MCS exhibits no cytotoxicity and good biocompatibility. ABZ was effectively loaded into the mesopores in an amorphous state, and marked improvements in its dissolution kinetics were observed after loading. Drug release behaviors were well simulated by the Weibull function.



## 1. Introduction

In the current study, a new preparation procedure is reported to prepare mesoporous carbon spheres (MCS) for drug delivery applications. MCS is first synthesized from a stirring step to generate glucose/silica composites in one pot, after which carbonization is performed to achieve the carbon spheres. This method is straightforward and high-yielding because all of the reagents are reacted in one pot and the carbon source, glucose, is completely converted into carbon spheres by evaporating the solvent from the solution. The method proposed is cost-effective because it is surfactant-free and the carbon source is inexpensive. The carbon spheres we obtained featured a large surface area and pore volume as well as excellent biocompatibility. More importantly, the product of this method can efficiently improve the solubility and dissolution of the model drug, ABZ, thereby revealing its potential use in drug delivery systems [1,2]. Then the influence of the structural characteristics of MCS on ABZ solubility and dissolution has been investigated. Finally, the Weibull function is used to investigate the release kinetics of ABZ from various ABZ/MCS formulations. To the best of our knowledge, no study has yet reported the characteristics of ABZ release from a similar material using the Weibull function.

## 2. Materials and methods

The formation scheme of MCS is shown in Fig. 1. Typically, adequate silica was added to 5 mL glucose aqueous solution at 30 °C under stirring to achieve a glucose /silica mass ratio of 1.5:1. After carbonization at 900 °C for 3 h, washing and drying, the obtained product was denoted as MCS-3. Similar steps were performed for MCS-1 and MCS-2 by changing the mass ratio of glucose/silica to 0.5:1 and 1:1. The A549, BEL-7402, and SGC7901 cell lines were selected to assay MCS-3 by standard 3-(4,5-dimethylthiazole)-2,5- diphenyltertraazolium bromide (MTT). ABZ/MCS formulations were prepared by adding MCS (0.2 g) to an ABZ–acetic acid solution (50 mg/mL) under stirring. The resulting ABZ/MCS was dried under vacuum at 50 °C for 7 h. Dissolution testing was performed at 37 °C, 100 rpm. The dissolution medium was composed of 900 mL of simulated gastric fluid (SGF). 5 mL of dissolution medium were withdrawn at fixed time points and then analyzed by the UV at 295 nm. The dissolution medium in the vessel was quickly replenished with SGF.

$N_2$ sorption isotherms were measured with Micromeritics Tristar 3020. Scanning electron microscopy (SEM) was achieved with a LEO 1530VP. Differential Scanning Calorimetry (DSC) was analyzed by DSC-4000. X-ray diffractometry (XRD) patterns were recorded on a multipurpose diffractometer.

## 3. Results and discussion

As shown in Fig. 1, as the mass ratio of glucose/silica increases from 0.5 to 1, the SEM morphology of the samples changes from partly fragmented (MCS-1) to hollow spheres (MCS-2). When the mass ratio of glucose/silica is 1.5, a completely spherical

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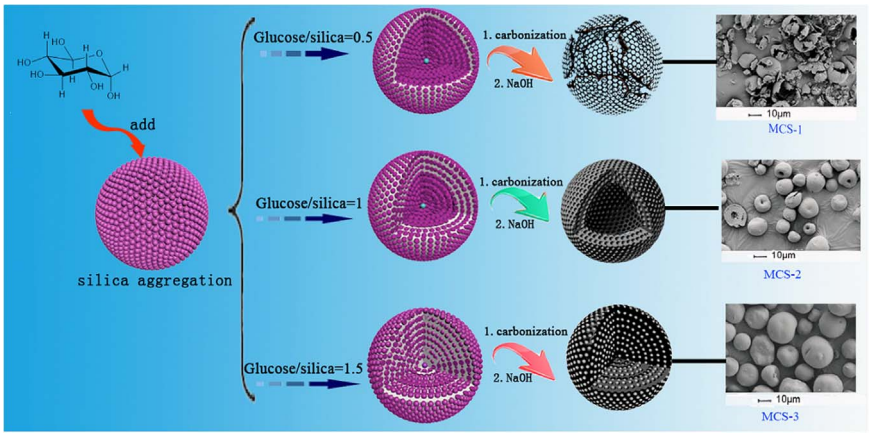


**Fig. 1.** The formation scheme and SEM images of MCS by the stirring method.

morphology (MCS-3) is observed. This result indicates that mass ratio of glucose/silica in a specific range affect the MCS morphology.

The $N_2$ adsorption isotherms (Fig. 2) for the carbon materials exhibit type IV curves with capillary condensation at a $P/P_0$ of 0.6–0.9, which is the characteristic of mesoporous materials. The $S_{BET}$ values of MCS-1, MCS-2 and MCS-3 are 709, 971, and 1632 $m^2/g$, respectively. The corresponding $V_P$ and $D_p$ values are 1.59, 2.38, and 4.13 $cm^3/g$, and 7.6, 9.3, and 11.2 nm, respectively, indicating that increasing the mass ratio of glucose/silica can improve $S_{BET}$, $V_P$, and $D_p$ because increments in glucose may moderately restrain skeleton shrinkage to some extent. The $N_2$ sorption isotherms generally display sharp decreases in $N_2$ adsorption capacity after ABZ loading, which are reflected by decreases in $S_{BET}$ and $V_P$ (40.7, 64.8, 67.6 $cm^3/g$ and 0.33, 0.38, 0.41 nm, respectively). It confirms that ABZ is successfully loaded into the MCS pore channels. Pore diameters decrease after ABZ loading (Fig. 2) because of filling of larger mesopores, and the mesopore diameters centered at around 5.4 nm.

The XRD results for ABZ (Fig. 3A) exhibit high-intensity reflections with sharp peaks at 6.94°, 11.59°, 13.92°, 17.90°, and 24.69°, which are characteristic of the crystal form. Distinct crystalline peaks are not detected in any of the ABZ-free carriers, ABZ/MCS-2, and ABZ/MCS-3. The results reveal that the ABZ absorbed into the pores of MCS-2 and MCS-3 presents a non-crystalline state and that the pores of these two carriers limit ABZ recrystallization. The ABZ/MCS-1 diffractogram exhibits distinct patterns with decreasing diffraction peaks at 7.39°, 12.51°,18.04°, 24.67°, and 25.74°, indicating generation of a new crystal form of ABZ on MCS-1 because of accumulation of ABZ on the external surface of MCS-1. Without the restrictive effect of the pore walls of carriers due to framework collapse, drug molecules tend to recrystallize. The DSC of ABZ is characterized by two sharp melting endothermic peaks at 211.7 and 219.7 °C (Fig. 3B). The first peak is due to melting of ABZ, which is followed by rapid recrystallization of the melt. The second endothermic peak reveals that the formed microcrystals melt once more [3]. The DSC of ABZ/MCS-2, and ABZ/MCS-3 show no endothermic peak before 250 °C, thereby demonstrating that the ABZ loaded into the pores of MCS-2 and MCS-3 present a non-crystalline state because of the restrictive effects of the pore walls. The DSC of ABZ/MCS-1 shows a depression in the endothermic melting peak at 208.6 °C with a shoulder peak at 214.3 °C, which may be due to the formation of new low-melting crystal form of ABZ. This form could be further converted into a more stable form after melting, as evidenced by the second small shoulder endothermic peak. These findings further reveal that the ABZ molecules are packed on the external surface of MCS-1, which agrees with the XRD results.

The solubility study suggests that ABZ is practically insoluble in water ($5.39 \times 10^{-3}$ mg/mL). ABZ/MCS-1 presents a 3.16-fold increment ($17.01 \times 10^{-3}$ mg/mL) in aqueous drug solubility compared with that of pure ABZ (Fig. 4A). Remarkable improvements in the drug solubility of ABZ/MCS-2 ($43.87 \times 10^{-3}$ mg/mL, 8.14-fold increase) and ABZ/MCS-3 ($87.66 \times 10^{-3}$ mg/Ml, 16.26-fold increase) in comparison with that of ABZ are also observed. Crystalline ABZ molecules loaded into the pores of MCS are restricted by the confined space of the pores, thereby retaining ABZ in its amorphous disordered form. Thus, an increase in solubility of the ABZ/MCS formulations is achieved because of the low lattice energy (high Gibbs free energy) of the amorphous state [4]. In ABZ/MCS-1, some ABZ molecules are packed onto the carrier surface and recrystallize, resulting in relatively lower solubility compared with those of the other formulations. The difference in solubility between ABZ/MCS-2 and ABZ/MCS-3 may be attributed to the dispersibility of ABZ. The large specific surface area and pore volume of ABZ/MCS-3 initially leads to better soaking of the

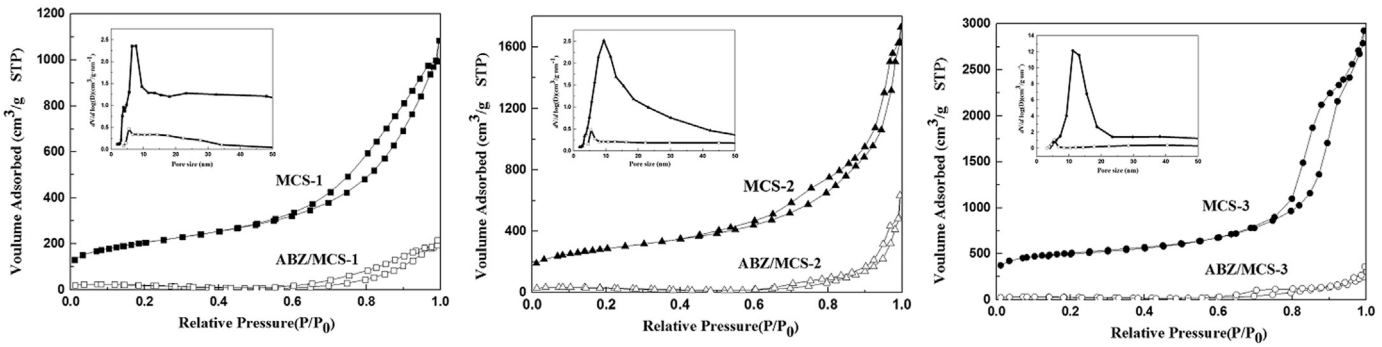


**Fig. 2.** Nitrogen sorption isotherms and pore diameter distributions of the samples before (solid) and after (hollow) ABZ loading.