

# Preparation of Porous Poly(lactic acid)/SiO<sub>2</sub> Hybrid Microspheres

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**ABSTRACT:** With 3-aminopropyltriethoxysilane (APTES) as coupling agent, poly(lactic acid) (PLA)/SiO<sub>2</sub> hybrid material was prepared to produce poly(lactic acid)/SiO<sub>2</sub> hybrid microspheres (PLAHs) with porous structure by the oil-in-water, single-emulsion solvent evaporation method. Field scanning electron microscopy results show that the PLAHs were porous microspheres about 20 μm in diameter. The holes in the PLAHs opened outside and were not complicated. A nitrogen adsorption-desorption experiment showed that the nitrogen adsorbed in the holes was easily desorbed, and the specific surface area of the PLAHs was calculated to be 6.87 m<sup>2</sup>/g according to the Brunauer-Emmett-Teller equation. Fourier transform infrared spectroscopy results show that PLA was amidated with APTES successfully and formed a kind of

organic-inorganic hybrid material by hydrolysis and condensation with tetraethoxysilane. Moreover, the molecular structure of the hybrid material was confirmed by X-ray photoelectron spectroscopy. Differential scanning calorimetry results show that the melting point of the PLAHs was higher than that of PLA by about 11.2°C. These PLAHs may be used in the controlled release of drugs by the embedding of the drugs in the holes of the PLAHs, and the drug loading amount can be controlled by the size and number of holes in the PLAHs. © 2006 Wiley Periodicals, Inc. *J Appl Polym Sci* 102: 679–683, 2006

**Key words:** composites; polysiloxanes; synthesis; drug delivery systems

## INTRODUCTION

Poly(lactic acid) (PLA) has been widely studied as a biomaterial because of its good biocompatibility and biodegradability.<sup>1</sup> PLA has good mechanical properties, which are comparable to today's standard packaging polymer polystyrene.<sup>2</sup> Moreover, the advantages of PLA also include its availability from renewable resources and a reduction in carbon dioxide emissions generated during manufacturing compared to conventional commodity plastics.<sup>3</sup> However, some of the other properties, such as melt viscosity, impact factor, heat distortion temperature, and gas barrier properties, are frequently not good enough for various end-use applications,<sup>4</sup> and much research has been done to improve its properties.<sup>5–11</sup>

The solvent removal technique is one of the most popular methods for the preparation of microspheres from hydrophobic polymers. The solvent removal technique can be divided into solvent evaporation, solvent extraction, spray-drying, and supercritical fluid technology.<sup>12–15</sup> On the basis of the solvent evapora-

tion technique, the oil-in-water, single-emulsion solvent evaporation method has been used to prepare microspheres and nanospheres of biodegradable polymers for drug delivery.<sup>16–19</sup> Furthermore, the water-in-oil-in-water emulsion solvent evaporation method has been used to prepare PLA microspheres.<sup>20,21</sup>

Described in this article is the preparation of poly(lactic acid)/SiO<sub>2</sub> hybrid microspheres (PLAHs) with porous structure by the oil-in-water, single-emulsion solvent evaporation method. In this process, PLA was amidated with 3-aminopropyltriethoxysilane (APTES) and formed a kind of organic-inorganic hybrid material by hydrolysis and con-condensation with tetraethoxysilane (TEOS); it was then dissolved in dichloromethane (DCM) to form an oil phase, which was dispersed into a water phase in the presence of the emulsifiers polyvinyl alcohol (PVA) and polysorbate 80 (Tween-80) in succession. After the organic solvent was removed by evaporation, the porous PLAHs were prepared. Although the oil-in-water, single-emulsion solvent evaporation method is a common technique for preparing microspheres and nanospheres, few investigations have been done on the preparation of porous PLAHs by this technique thus far. By the introduction of SiO<sub>2</sub> into the PLA chain, the heat stability and strength of PLA can be improved. In addition, the hydrophilicity of PLA can be improved because of —OH groups on SiO<sub>2</sub>. Therefore, many properties, including heat stability, strength, hydrophilicity, and

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degradability, of PLAHS can be controlled by the adjustment of the proportion of PLA and SiO<sub>2</sub>.

## EXPERIMENTAL

### Materials

TEOS with analytical purity (SiO<sub>2</sub> ≥ 28.4%) and PVA (1750 ± 50) were obtained from Chemical Medical (Group) Shanghai Chemical Reagent Cooperation, Shanghai City, China. APTES was obtained from Nanjing Crompton Shuguang Organosilicon Specialties Co., Ltd., Nanjing City, China. We prepared PLA (viscosity average molecular weight (*M<sub>v</sub>*) = 8.0 × 10<sup>4</sup>). SnCl<sub>2</sub>·2H<sub>2</sub>O was purchased from Liuzhou Smeltery. Polysorbate 80 (Tween 80) was purchased from Shantou Xilong Chemical Co., Ltd., Guangdong Province, China. DCM was purchased from Tianjin Damao Chemical Factory. Tetrahydrofuran (THF) was purchased from Yixing Zhanwang Chemical Factory, Jiangsu Province, China.

### Sample preparation

#### PLA/SiO<sub>2</sub> hybrid material

With SnCl<sub>2</sub>·2H<sub>2</sub>O as a catalyst, 1 g of PLA was amidated with 1 mL of APTES in 10 mL of THF at 55°C for 2.5 h in a four-necked, round-bottom flask; then, 1 mL of TEOS was added. When the system temperature was cooled to 30°C, 0.2 mL of H<sub>2</sub>O was dropped in. With HCl catalyzed, the PLA amidated with APTES was hydrolyzed and con-condensed with TEOS at 30°C for 4.5 h. When the byproducts were removed by vacuum, the PLA/SiO<sub>2</sub> hybrid material was obtained.

#### PLAHS

To produce the water phase, 0.2 g of PVA was dissolved in 40 mL of H<sub>2</sub>O; then, 0.1 g of Tween 80 was added, and the solution was mixed evenly.

To produce the oil phase, 1 g of PLA/SiO<sub>2</sub> hybrid material was dissolved in 10 mL of DCM.

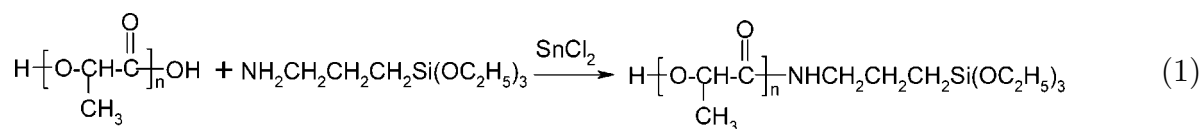
To prepare the oil-in-water emulsion, 10 mL of the oil was dropped in 40 mL of the water solution with a stirring at speed of 500 rpm at 20°C for about 10 min. Fifteen minutes later, the temperature was raised and kept above 40°C until the organic solvent DCM evaporated completely; then, by centrifugal separation, water washing, and vacuum drying separately, the PLAHS with porous structure were obtained.

Field scanning electron microscopy photographs were taken with a Jeol (Jeol, Japan) JSM-6700F field scanning electron microscope (10 kV). The sample was ultrasonically dispersed in ethanol for 30 min and then dropped on a copper pallet and dried, and gold was evaporated. The nitrogen adsorption-desorption experiment was performed at 77 K with a Beckman Coulter (Florida, USA), SA 3100. The specific surface area value was calculated according to the Brunauer-Emmett-Teller (BET) equation at a gas pressure (*P*)/saturated vapor pressure (*P*<sup>0</sup>) between 0.05 and 0.2. Fourier transform infrared (FTIR) spectra were measured with a Nicolet (Wisconsin, USA) Nexus-870 with KBr pellets. X-ray photoelectron spectroscopy (XPS) was performed with Mg Kα radiation from a VG (West Sussex, UK) ESCALAB MKII X-ray photoelectron spectrometer. Differential scanning calorimetry (DSC) was conducted with a Mettler Toledo (Im Langacher, Switzerland) DSC-821E at a scanning rate of 10°C/min under a nitrogen atmosphere at a flow of 80 mL/min.

## RESULTS AND DISCUSSION

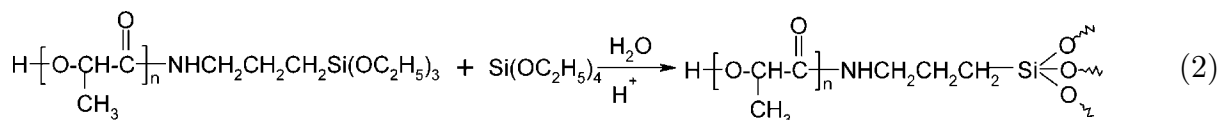
### PLA/SiO<sub>2</sub> hybrid mechanism

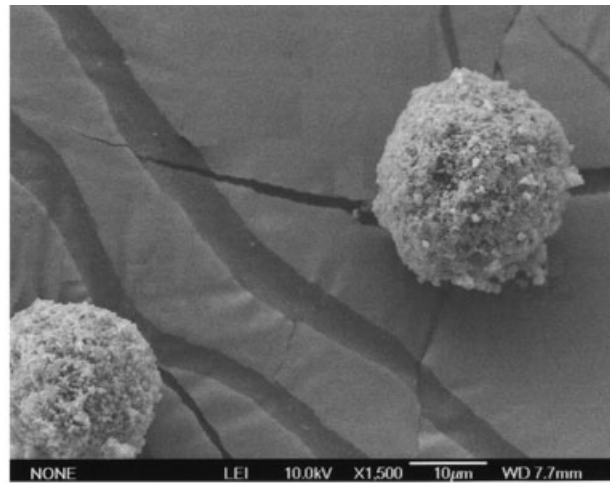
With SnCl<sub>2</sub>·2H<sub>2</sub>O as a catalyst, PLA was amidated with APTES in THF as follows:



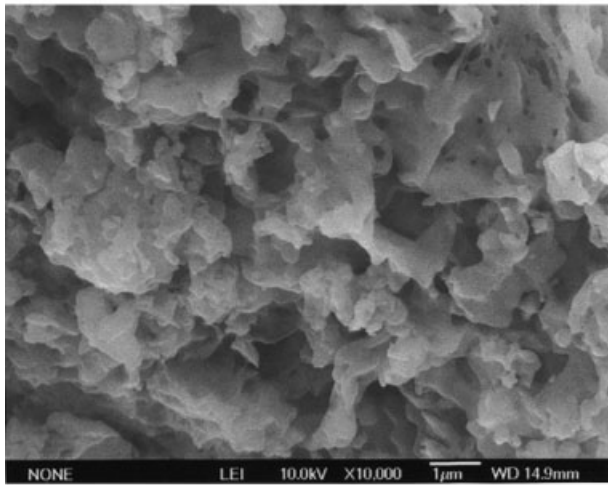
When PLA was amidated with APTES, the ethoxy groups of APTES were not affected. In the presence of the HCl catalyst, these ethoxy groups were hydro-

lyzed and con-condensed with TEOS to form the PLA/SiO<sub>2</sub> hybrid material, and the hybrid reaction equation is as follows:

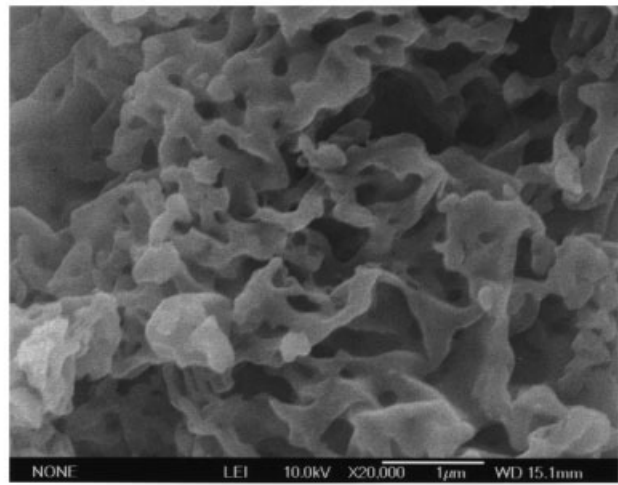




(a)



(b)



(c)

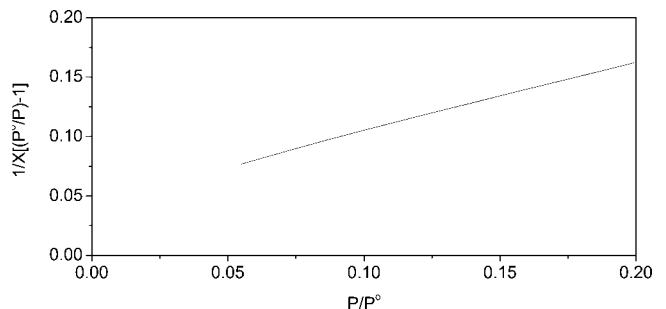
**Figure 1** Field scanning electron microscopy photographs of the samples: (a) PLAHs (300×), (b) PLAHs surface (10,000×), and (c) PLAHs surface (20,000×).

**Morphology of the microspheres**

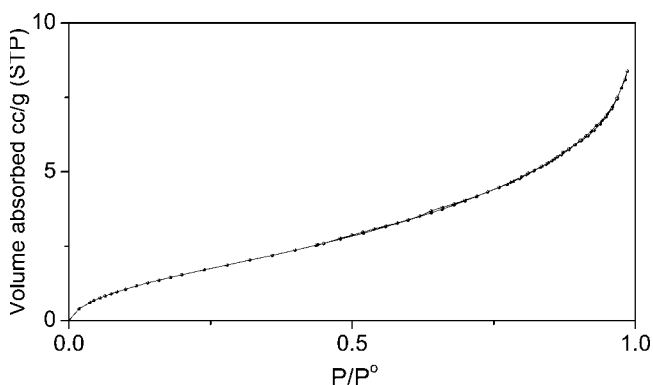
The PLAHs were successfully prepared by the oil-in-water, single-emulsion solvent evaporation as shown in Figure 1(a). The PLAHs were about 20 µm in diameter. Figure 1(b,c) shows that the PLAHs were porous in structure. Interestingly, almost all holes opened outside, as shown clearly in Figure 1(c), which would be convenient for drug embedding. Figure 2 shows the nitrogen adsorption–desorption isotherm for the PLAHs. The desorption isotherm curve nearly overlapped with the adsorption isotherm curve. This behavior signified that the nitrogen adsorbed in the holes was easily desorbed, which implies that the holes in the PLAHs have opened outside and were not very complicated. This result agrees well with the morphology, as shown in Figure 1(c). The specific surface area of the PLAHs was calculated on the basis of the BET equation. A

convenient form of the BET equation<sup>19</sup> may be written as

$$1/X[(P^\circ/P) - 1] = 1/X_m C + (C - 1/X_m C)P/P^\circ \quad (3)$$



**Figure 2** Nitrogen adsorption–desorption isotherm for PLAHs.

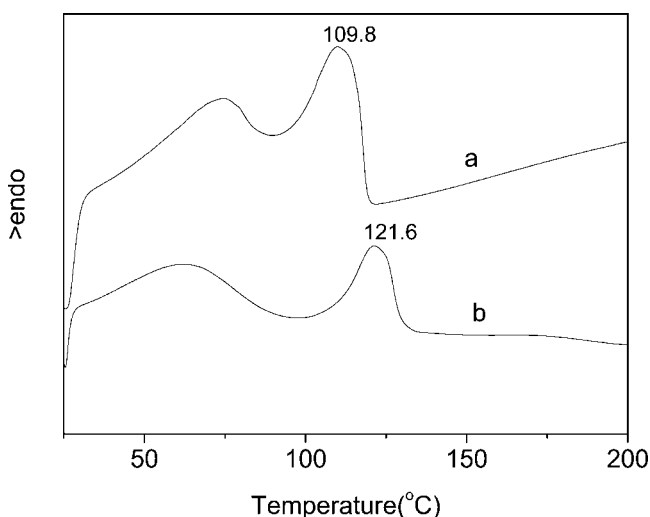


**Figure 3** BET for the nitrogen adsorption plot of the PLAHS.

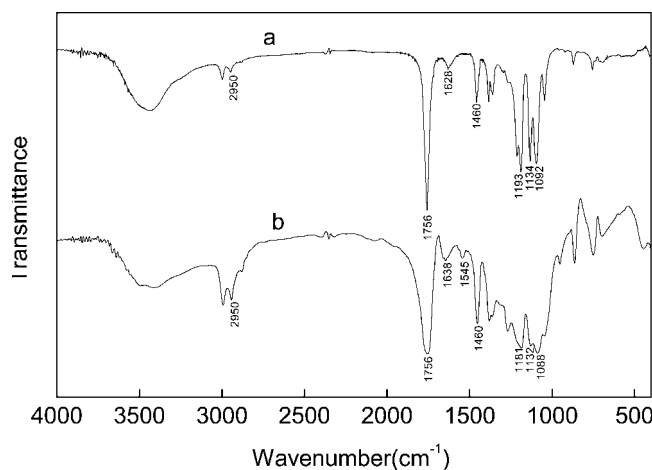
where  $X$  is the amount of gas adsorbed at relative pressure  $P/P^0$ ,  $X_m$  is the monolayer capacity, and  $C$  is a constant. The BET equation gives a linear relationship between  $1/X[(P^0/P) - 1]$  and  $P/P^0$ , and the range of linearity is usually restricted to a limited part of the isotherm. The BET for nitrogen adsorption plot of the PLAHS is shown in Figure 3; the slope and intercept were 0.5880 and 0.0457, respectively, which allowed us to calculate  $X_m$ . The specific surface area was calculated with the BET method to be  $6.87 \text{ m}^2/\text{g}$ . It is interesting that this characteristic structure may be used in the controlled release of drugs by the embedding of the drugs in the holes in the PLAHS, and the drug loading amount can be controlled by the size and number of holes in the PLAHS.

### FTIR analysis

Figures 4(a,b) shows the FTIR spectra of PLA and the PLAHS. In Figure 4(a), the characteristic peaks for PLA



**Figure 4** FTIR spectra of the samples: (a) PLA and (b) PLAHS.

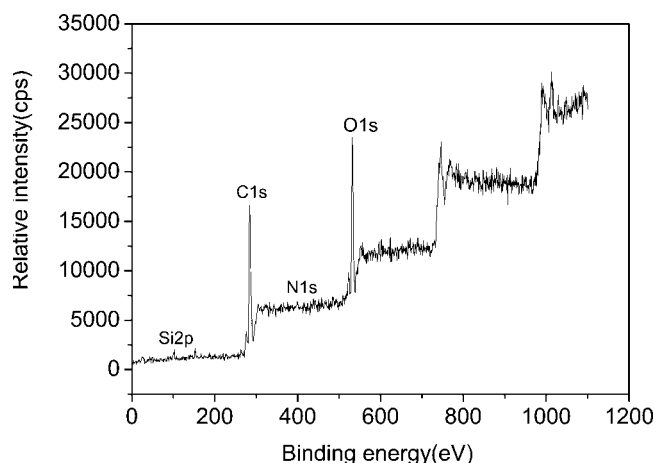


**Figure 5** XPS full-scan spectrum of the PLAHS.

are shown:  $\nu\text{C}=\text{O}$  at  $1756 \text{ cm}^{-1}$ ,  $\nu\text{C}=\text{O}$  at  $1628 \text{ cm}^{-1}$ ,  $\nu_{\text{as}}\text{C}-\text{O}-\text{C}$  at  $1134 \text{ cm}^{-1}$ ,  $\nu_{\text{s}}\text{C}-\text{O}-\text{C}$  at  $1193$  and  $1092 \text{ cm}^{-1}$ ,  $\nu(-\text{CH}_3)$  at  $2950 \text{ cm}^{-1}$ , and  $\delta(-\text{CH}_3)$  at  $1460 \text{ cm}^{-1}$ . In the case of the FTIR spectrum of PLAHS presented in Figure 4(b), the presence of  $-\text{CONH}-$  identified for the following characteristic vibrations were found:  $\nu\text{C}=\text{O}$  at  $1638 \text{ cm}^{-1}$  and  $\delta\text{N}-\text{H}$  at  $1545 \text{ cm}^{-1}$ , which implies that PLA was amidated with APTES successfully. Moreover, the characteristic peaks for the formation of the  $\text{Si}-\text{O}-\text{Si}$  bands  $\nu\text{Si}-\text{O}-\text{Si}$  at  $1132$  and  $1088 \text{ cm}^{-1}$  and the characteristic peak of  $\text{Si}-\text{C}$  at  $1181 \text{ cm}^{-1}$  are also shown in Figure 4(b), which overlapped  $\nu_{\text{as}}\text{C}-\text{O}-\text{C}$  and  $\nu_{\text{s}}\text{C}-\text{O}-\text{C}$  and became broad, which implies that the PLA amidated with APTES hydrolyzed and con-condensed with TEOS and formed PLAHS. Many researchers have reported the hydrolysis and cocondensation between TEOS and APTES.<sup>22–24</sup>

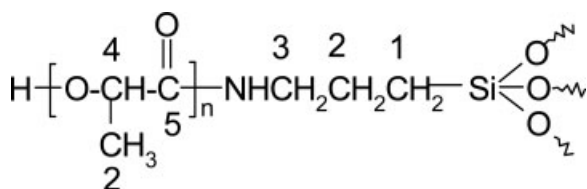
### XPS analysis

Figure 5 illustrates the XPS full-scan spectrum of the PLAHS. In Figure 5, the peaks  $\text{Si}2p$ ,  $\text{C}1s$ ,  $\text{N}1s$ , and



**Figure 6** Curve-fitted XPS  $\text{C}1s$  spectrum of the PLAHS.

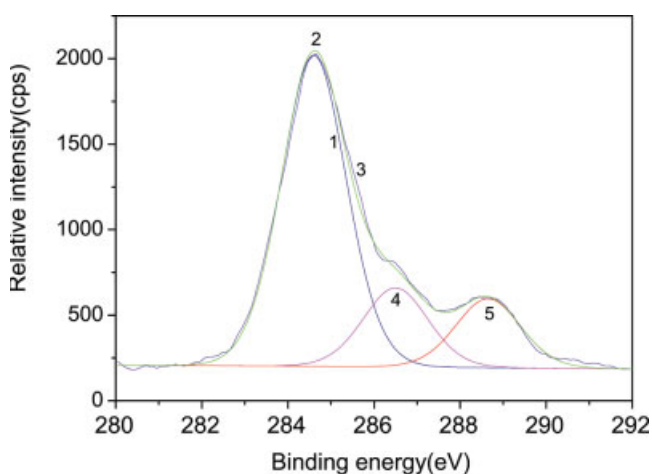
O1s are at 101.55, 285.05, 400.21, and 532.05 eV, respectively. When the peak C1s was fitted, five peaks at 284.61, 284.64, 284.67, 286.50, and 288.60 eV were obtained, as shown in Figure 6, corresponding to six different carbons (C1 ~ C5) in the PLAH molecular structure as following:



Peaks Si2p, C1s, N1s, and O1s proved that the PLAHs were made up of Si, C, N, and O elements, which implies that PLA was amidated with APTES successfully and formed a kind of organic-inorganic hybrid material by hydrolysis and con-condensation with TEOS in the synthesis of PLAHs. Moreover, peak C5 provided evidence of the existence of amide bonds in the molecular structure. This fact agrees well with the conclusions drawn from FTIR analysis.

**DSC analysis**

Figure 7 is the DSC heating scan of PLA and the PLAHs. The peak at about 109.8°C in Figure 7(a) corresponds to the melting of PLA. Another peak at about 121.6°C in Figure 7(b) corresponds to the melting of the PLAHs. It was obvious that when PLA was amidated with APTES and hybridized with TEOS, the melting point was increased by about 11.2°C. The endothermic peaks before 109.8 and 121.6°C corresponded to the evaporation of DCM and H<sub>2</sub>O.



**Figure 7** DSC curve of the samples: (a) PLA and (b) PLAHs. [Color figure can be viewed in the online issue, which is available at [www.interscience.wiley.com](http://www.interscience.wiley.com).]

**CONCLUSIONS**

With APTES as a coupling agent, PLA was amidated with APTES successfully and formed PLA/SiO<sub>2</sub> hybrid material by hydrolyzing and con-condensing with TEOS. The porous PLAHs, sized about 20 μm in diameter, were prepared by the oil-in-water, single-emulsion solvent evaporation method. The holes in the PLAHs opened outside and were not very complicated. According to the BET equation, at *P/P*<sup>0</sup> values between 0.05 and 0.2, the specific surface area of the PLAHs was calculated to be 6.87 m<sup>2</sup>/g. These characteristic holes would be convenient for the embedding of drugs and may be used in the controlled release of drugs. Moreover, the melting point of the PLAHs was higher than that of PLA by about 11.2°C.

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