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Selecting water-alcohol mixed solvent for synthesis of polydopamine nano-spheres using solubility parameter

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The solvent plays an important role in a given chemical reaction. Since most reaction in nature occur in the mixed-solvent systems, a comprehensive principle for solvent optimization was required. By calculating the Hansen solubility parameters (HSP) distance R_a , we designed a model experiment to explore the influence of mixed solvents on the chemical synthesis. The synthesis of polydopamine (PDA) in the water-alcohol system was chosen as model. As predicted, the well-dispersed PDA spheres were obtained in selected solvents with smaller R_a values: methanol/water, ethanol/water and 2-propanol/water. In addition, the mixed solvent with smaller R_a values gave a higher conversion of dopamine. The strategy for mixed solvent selection is might be useful to choose optimal reaction media for efficient chemical synthesis.

The solvent, which makes up approx. 90% of the total mass of a reaction solution, plays an important role for a solution based chemical reaction. Solubility, equilibrium position and reaction rate are all affected by solvent¹. Solvent selection continues to be one of the most challenging issues for current synthetic chemistry since most of chemical or biochemical reactions on the earth occur in wet environment². Based on the principle of “like dissolves like”, the single solvent system is the primary choice for chemical synthesis. However, most, if not all, reactions in nature occur in mixed-solvent systems. Up to now, the mixed solvent system has been widely used for many years, especially in the coating industry³. For example, using solvent selection by computer programs, one can now easily predict how to dissolve a given polymer in a mixture of two solvents, neither of which can dissolve the polymer by itself. Though mixed solvents have been used in synthetic chemistry, few investigations have focused on how to select mixed solvents.

Water and ethanol are versatile solvents, and the water-ethanol system has been broadly used. For example, mixtures with different fraction of ethanol have been used as alcoholic beverages. Another interesting example is that using 70 percent alcohol is a better disinfectant against the tubercle bacillus than using pure alcohol⁴. Recently, Zhang et al. developed a mixed-solvent strategy for efficient exfoliation of inorganic graphene analogues (IGAs), e.g., MoS₂, WS₂ and BN⁵. In this article, the authors demonstrated how two “poor” solvents, ethanol and water, can be designed to give high solubility to various IGAs.

Messersmith and co-workers demonstrated that dopamine self-polymerization was a powerful approach to apply multifunctional coatings onto various surfaces, including noble metals, metal oxides, ceramics, and polymers. These coatings would be served as an adhesion layer to immobilize biological molecules⁶. Consequently, several PDA-based systems have emerged as powerful tools to address many various challenging surface problems^{7–12}. More recently, the monodisperse polydopamine (PDA) spheres have been directly synthesized in a water-alcohol mixed solvent at room temperature. The results revealed that the volume ratio of water to alcohol strongly influenced on the synthesis of the PDA spheres¹³. Lu and co-workers prepared PDA spheres by use of about 29% ethanol as the solvent¹⁴. To our knowledge, there was a lack of a comprehensive principle that applied to select the volume ratio of water to alcohol for PDA synthesis. Inspired by the above results, we therefore designed the experiments to explore the influence of solvent on the synthesis of PDA spheres in the water-ethanol system.

The theory of Hansen solubility parameters (HSP) is a semi-empirical correlation developed to explain dissolution behaviour¹⁵. Briefly, HSP formula usually has the symbols δ_D , δ_P , and δ_H , which are the dispersive, polar, and hydrogen-bonding solubility parameters, respectively, and are sometimes replaced by D , P , and H , for convenience. The dissolution process is an adaptation between the HSP parameters of solvents and solutes. The HSP distance R_a is used to evaluate the level of adaptation and R_a can be calculated by equation (1).

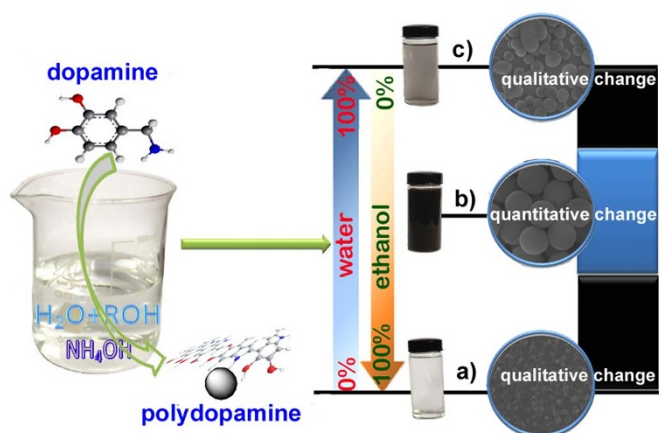


Figure 1 | Synthesis of polydopamine in the water-alcohol mixed solvents. Photograph and SEM images of polydopamine in (a) pure ethanol, (b) the ethanol-water mixed solvent with the volume ratio of 30%, and (c) pure water, respectively.

$$R_a = [4(D_{solv} - D_{solu})^2 + (P_{solv} - P_{solu})^2 + (H_{solv} - H_{solu})^2]^{0.5} \quad (1)$$

The smaller the R_a value, the higher the expected solubility. In addition to single-component solvents, HSP theory can be also applied to mixed-solvents, in which each of the three HSP parameters for a solvent mixture is a linear function of composition, calculated by equation (2).

$$D(P,H)_{blend} = \sum \phi_{n,comp} D(P,H)_{n,comp} \quad (2)$$

where ϕ is the volume fraction for each composition. Therefore, equation (1) and (2) enable us to predict the solubility of different chemicals in various mixed-solvents, which effectively allows us to design ideal solvent systems.

Before conducting experiments for the synthesis of PDA, R_a values between different solvent mixtures and dopamine were calculated using equation (1) and (2). More details are given in the Supporting Information (see Supplementary Materials online).

Results & discussion

Figure 1 shows the results of experiments performed in the water-ethanol mixed solvents. PDA spheres could not be formed in pure ethanol (Figure 1a), but the PDA spheres could be obtained in the mixed-solvents made with water and ethanol or pure water (Figure 1b and 1c). Monodisperse PDA spheres could be synthesized only at an appropriate ratio of ethanol/water.

To verify the influence of solvent, we conducted the experiments to synthesize PDA in various water-ethanol mixed solvents. Figure 2 shows that the synthesis of PDA is strongly dependent on the volume fraction of ethanol in water. As shown in Figure 2c–f, the well-dispersed PDA spheres were obtained in the mixed solvents with the volume fractions of ethanol from 25% to 40%. We calculated the R_a between dopamine and ethanol/water mixtures using equations (1) and (2) based on the data listed in Table S1. Interestingly, these mixed solvents all have smaller R_a value (Table S2). In contrast, it was difficult to obtain well-dispersed PDA spheres in those mixed solvents with high R_a values. We also investigated the conversion of dopamine in the mixed solvents and found that a smaller R_a value gave a higher conversion (Table S5). Together, it seemed that the well-dispersed products with higher conversions tend to be prepared in the “good” solvents for the reactants.

It was worth mentioning that the concentration of ammonia had a dramatic effect on controlling the size of PDA spheres, but no effect on the morphology and yield of PDA sphere (Figure 3), consistent with previous reports¹⁴.

This alcohol-water system was not only limited to ethanol, other alcohols such as methanol or 2-propanol with smaller R_a were both proven to be efficient solvent systems. The R_a values between dopamine and methanol (or 2-propanol)/water mixtures are listed in Table S3 and S4. As predicted, the well-dispersed PDA spheres were obtained in 10% or 20% of methanol or 40% 2-propanol with smaller R_a (Figure 4). Based on the analysis of the data, it was found that in all the three mixed solvent system the solvents with the smallest R_a gave the highest percent conversion of dopamine (ρ), as shown in Tables S5–S7. It should be pointed that the ρ was calculated via the weight ratio of PDA to DA and the morphology was ignored. Under optimum experiment conditions the ρ in methanol, ethanol and

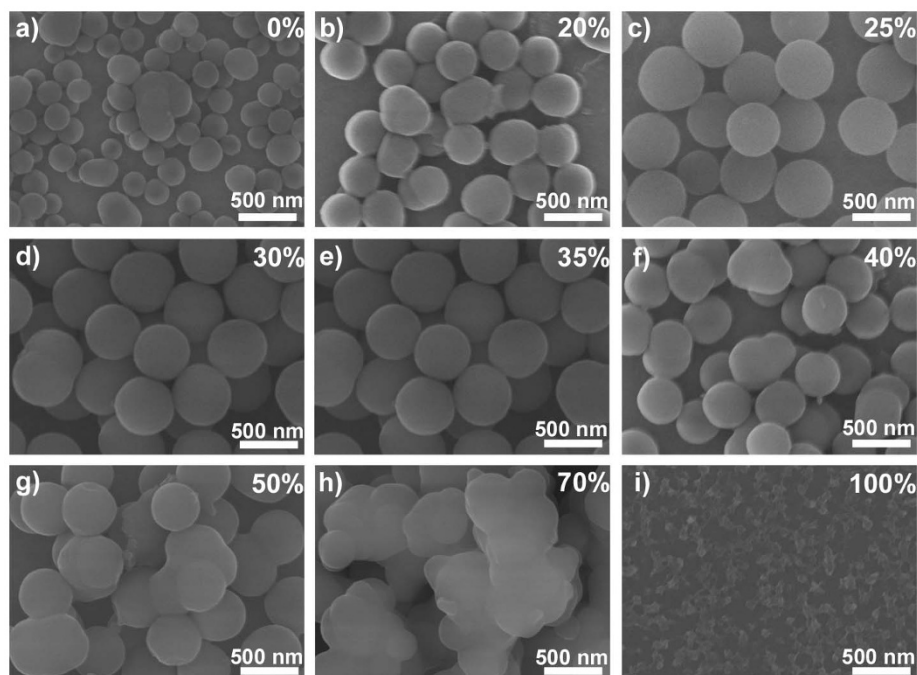


Figure 2 | SEM images of PDA obtained in various ethanol/water mixtures. The volume fractions of ethanol are (a) 0%, (b) 20%, (c) 25%, (d) 30%, (e) 35%, (f) 40%, (g) 50%, (h) 70%, and (i) 100%, respectively. The scale bars are 500 nm.

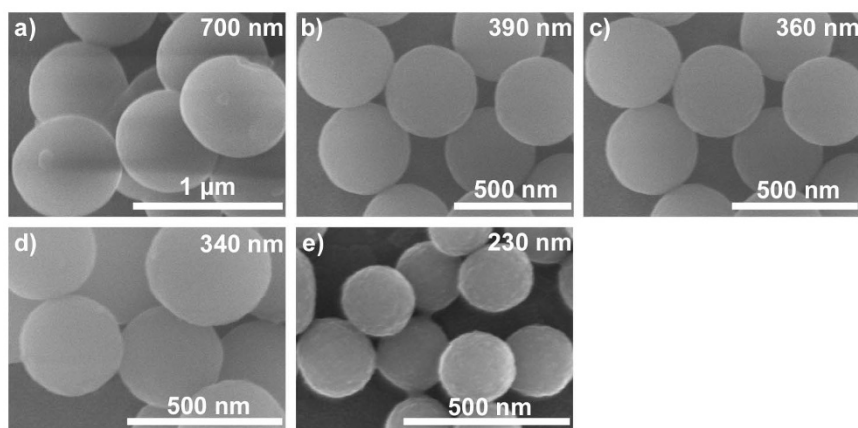


Figure 3 | SEM images of PDA spheres with different diameters prepared at different concentration of ammonia, (a) 0.1, (b) 0.17, (c) 0.2, (d) 0.28, and (e) 0.35 mL (28–30%). The volume fractions of ethanol are all 30%.

2-propanol-water system with smallest R_a was 50.57%, 40.25%, and 37.18%, respectively (Table S8). The yield of PDA spheres in methanol-water mixed solvent could even reach more than 50%, indicating that the organic component of the mixed solvents is the main influence factor for the conversion of dopamine when using different solvents. Figure S1 and Figure S2 show the SEM images of PDA prepared in different methanol/water and 2-propanol/water mixtures. The PDA products tended to be assembled together in the solvents with higher R_a .

The theory of chemical equilibrium may facilitate the understanding of this concept. The concentrations of the reactants or products do not affect the equilibrium constant, but does affect the equilibrium position¹⁶. For example, a decrease in concentration of the products causes the equilibrium to shift to the side of product. In other words, if the solvent can dissolve the reactants better than the products, the equilibrium will also tend to generate products. Apparently, the solubility of solvent is very important for chemical synthesis.

In summary, we demonstrated that the PDA spheres could be more easily obtained in the weakly alkaline alcohol-water mixed solvents with smaller R_a . Although the synthesis of PDA spheres in alcohol-water mixed solvents has been reported earlier^{13,14}, the present report is the first example of the application of HSP theory for the prediction of the PDA synthesis in alcohol-water mixed solvents. This empirical formula might be useful to predict other reaction

media in chemical synthesis. Further, with the aid of computers, more complex solvents with smaller R_a for reactants can be designed for synthesis. We expect to extend the selection of mixed solvents to other synthesis in inorganic, organic and biologic chemistry.

Methods

Materials. Dopamine hydrochloride (DA) was purchased from Acros Organics (New Jersey, USA). Ammonia aqueous solution, methanol, ethanol, and 2-propanol were obtained from J&K Scientific Ltd (Shanghai, China). Other chemical reagents were of analytical grade and were obtained commercially. All the solutions were prepared with Milli-Q purified water (Millipore, ≥ 18.2 M Ω cm).

Preparation of PDA nano-spheres. The synthesis of PDA spheres was carried out in a water-alcohol mixed solvent. The alcohol (methanol, ethanol, or 2-propanol) was mixed with water and the volume of the mixed solvent was fixed at 40.0 mL. Ammonia aqueous solution (NH₄OH, 0.20 mL, 28–30%) was added to the alcohol/water mixtures under mild stirring at room temperature for 30 min. Finally, dopamine hydrochloride was directly added to the mixed solution. The color of this solution immediately turned to pale brown and gradually changed to dark brown. The reaction was allowed to proceed for 30 h according to the literature¹⁴. The product was centrifuged and washed with water and anhydrous ethanol for three times. The product was dried in vacuum overnight at 60°C was used to calculate the conversion of dopamine.

Characterization. Field-emission SEM (Hitachi S4800) was used study the morphology of the products.

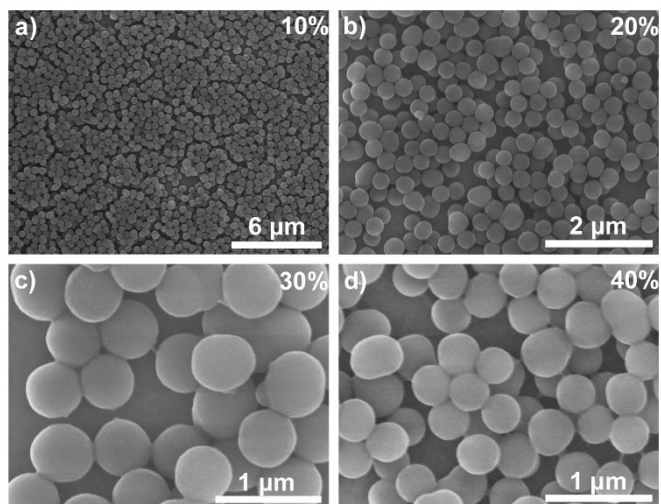


Figure 4 | SEM images of PDA obtained in (a), (b) methanol/water and (c), (d) 2-propanol/water mixtures.

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Author contributions

X.J. performed the most of experiments, collected and analyzed the data. Y.W. wrote the main manuscript text and prepared all figures in text. M.L. conceived the experiments, analyzed results, and wrote the paper.

Additional information

Supplementary information accompanies this paper at <http://www.nature.com/scientificreports>

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SCIENTIFIC REPORTS

OPEN **Corrigendum: Selecting water-alcohol mixed solvent for synthesis of polydopamine nano-spheres using solubility parameter**

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This Article contains errors in Figs 2 and 3. Figure 2d was inadvertently duplicated in Fig. 2e; Fig. 3c was inadvertently duplicated in Fig. 3b. The correct Figs 2 and 3 appear below as Figs 1 and 2 respectively.

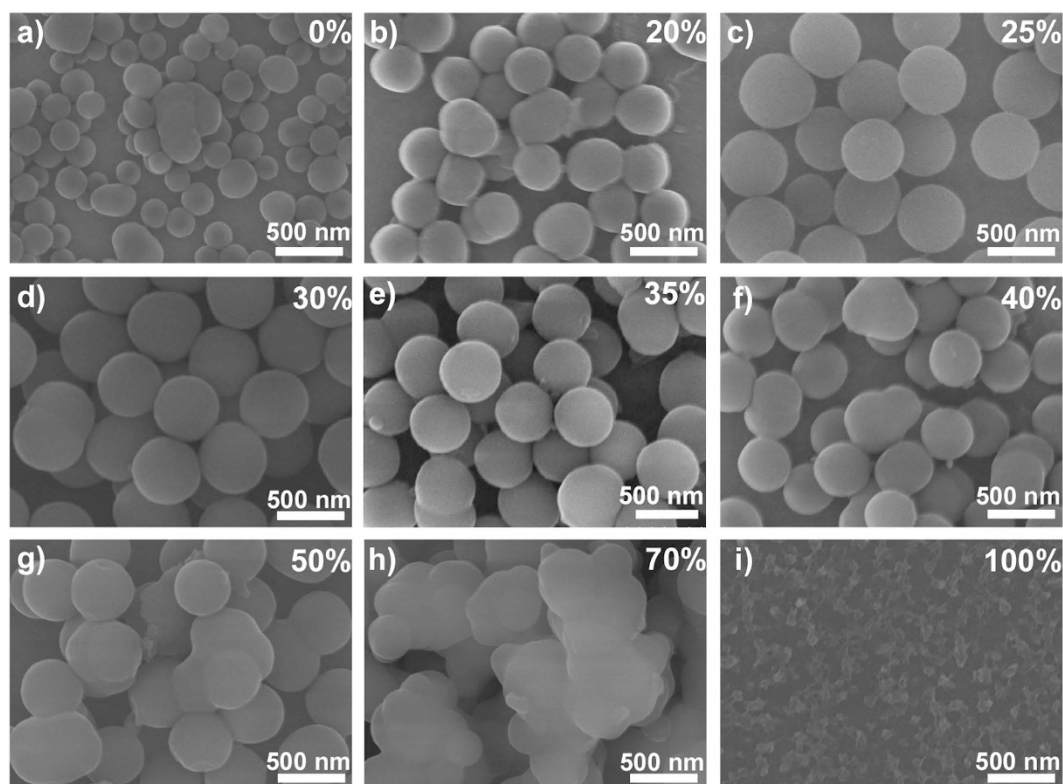


Figure 1.

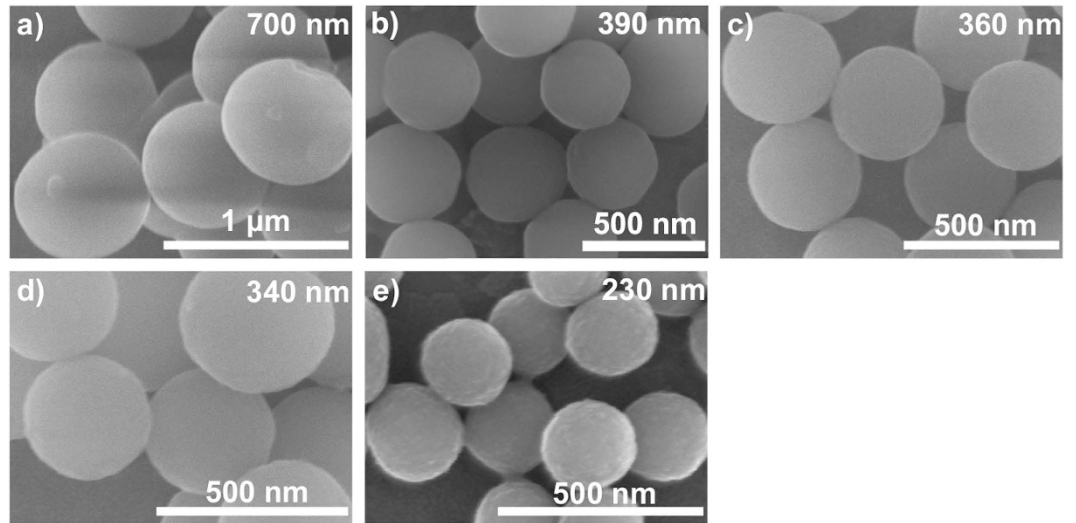


Figure 2.



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