Helical silver(I)-glutathione biocoordination polymer nanofibres

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Helical nanofibres of silver(I)-glutathione (Ag-GSH) biocoordination polymer (BCP) are fabricated by introducing dimethyl sulfoxide into the mixture solution of Ag⁺ ions and L-GSH molecules. The prepared BCP nanofibres show hierarchical helical structures, which are constructed via twisting of small fibres. Water-soluble helices could be further cross-linked with Ca²⁺ ions to form a well-dispersed aqueous suspension. When gold nanorods are adsorbed onto these helical nanofibres, the unique plasmon-induced circular dichroism characteristic is observed in the region of the local surface plasmon resonance of gold nanorods. This type of chiroptical metamaterials may have promising applications in nonlinear optics, negative refraction and biosensing.

1. Introduction

Coordination polymers (CPs), a novel type of functional materials constructed by metal nodes and organic bridging ligands, have attracted much scientific interest and hold the potential to be engineered for a wide range of applications such as gas separation and storage [1,2], catalysis [3], sensing [4] and biomedicine [5,6], owing to an essentially limitless choice of building blocks. By scaling down to the nanometre region, some size- and morphology-dependent properties of CPs have been appearing [7,8]. Yet, challenges remain in design and preparation of the functional nanoscale coordination polymers (NCPs) that meet the stringent requirements of biological systems. Guided by this, biomolecules are introduced into NCPs to replace conventional synthetic molecules (this class of NCPs is called bio-CPs, BCPs) [9–13]. The big driving force to study BCPs is that, compared with non-biological chiral components, biomolecules can not only provide multiple possible metal binding nodes but also
confer chirality, specific biorecognition or self-assembly capabilities to NCPs [14]; moreover, they have good biocompatibility and are environmentally friendly. These remarkable properties give rise to bulk production of biologically and environmentally compatible NCPs, which are easily incorporated into biological systems. Selecting natural amino acids as an example, the primary structures of 20 amino acids (except glycine) in biology are chiral and exclusively in their L-forms, which are selectively recognized and further assembled into proteins. The homochirality of amino acid building blocks not only determines the nature of higher-order structures in the proteins (e.g. the right-handed $\alpha$-helix (secondary structure) and the $\beta$-fold (tertiary structure)) but can also translate molecular scale chiral information into nanoscale architectures, and then develop into the macroscopic behaviour of three-dimensional frameworks through hierarchical assembly [15–17].

Hierarchical assembly exists abundantly in biological systems as well as in synthetic molecules or nanomaterials, facilitating formation of well-defined functional aggregates without synthesizing the whole entities via the bond-by-bond way. And many hierarchical assemblies have been demonstrated for constructing functional materials, devices or systems, ranging from assemblies of peptides [18], amphiphiles [15], polymers [19] and coordination supramolecules [20], to name a few. However, for NCPs, especially BCPs, up till now, only a few hierarchical assemblies with unusual structures, particularly helical or chiral structures, have been fabricated [12,21], and preparation of BCPs with helical or chiral structures still remains a daunting challenge. Herein, a natural tripeptide, glutathione ($\gamma$-L-glutamyl-L-cysteinyl-glycine, L-GSH), is chosen as a bridging ligand to construct BCPs with Ag$^+$ ions, aiming at hierarchical assembly of helical BCP nanofibres. Notably, the helical Ag-GSH BCP nanofibres are formed by introducing specific amount of poor solvent dimethyl sulfoxide (DMSO) into an aqueous solution of Ag$^+$ ions and GSH. Moreover, after cross-linking by Ca$^{2+}$ ions, the Ag-GSH BCP nanofibres can maintain not only the helical structure but also improve the stability in aqueous solution. After combination with gold nanorods via electrostatic interaction, the BCP nanofibre-based composites show plasmon-induced optical activity in the local surface plasmon resonance (LSPR) region of gold nanorods.

2. Results and discussion

(a) Ag-GSH helical nanofibres: morphology and hierarchical assembly

Generally, the assembly process and products of BCPs are found to be susceptible to the reaction conditions, such as the precursor concentration and molar ratio, pH of the medium, reaction temperature, reaction time and type of solvent. Such is the case for the Ag-GSH system. Different from our previous work on synthesis of the Ag-GSH BCP hydrogel [22], the reaction conditions for preparation of the Ag-GSH BCP helical nanofibres were rationalized as follows: 0.75 mmol L-GSH and 0.45 mmol AgClO$_4$·H$_2$O were mixed in 9 ml aqueous solution at a pH of 6.0, and then 6 ml DMSO was added into the solution dropwise. Later, the mixture solution was transferred into an oven with a constant and fixed temperature at 37°C and kept undisturbed for 96 h.

Figure 1a, b and electronic supplementary material, figure S1, show the morphology of as-prepared helical nanofibres (denoted as Ag-GSH fibres). Several interesting features can be discerned. (i) The products are a mixture of the twisted and untwisted nanofibres. Some untwisted nanofibres are observed when the diameters of the nanofibres are smaller than 200 nm (see electronic supplementary material, figure S1b), whereas nearly all the nanofibres of diameter larger than 220 nm are twisted to form the helical structure (see electronic supplementary material, figure S1a). It is estimated that the ratio of the helical nanofibres is 80–90% in the final products. (ii) It is clear that the helical nanofibres are composed of several strands and formed by twisting together of the smaller ones (figure 1b). (iii) The helical nanofibres composed of Ag$^+$ cations and L-GSH peptide exclusively are of the right-handed structures. This phenomenon is
Figure 1. TEM images of the Ag-GSH helical nanofibres (a, b) before and (c, d) after cross-linking with Ca$^{2+}$ ions at different magnifications. A nanofibre consisting of two helical strands can be clearly discerned in (b).

analogous to our previous study on the system of Ag$^{+}$ cations and chiral cysteine molecules, in which the molecular chirality of amino acid could be delivered to the CPs and thus determine the configuration of the final nanostructures [12].

The assembly process of the helical nanofibres is monitored by scanning electron microscopy (SEM). Seen from figure 2, as the reaction time increases, the non-helical nanofibrils with small diameters of 52 ± 8 nm are firstly formed after 12 h of incubation at 37°C (figure 2a and electronic supplementary material, figure S3). Subsequently, the small fibrils continuously grow, and simultaneously start to twist with each other to form right-handed helical fibres, whereas the mean diameter of nanofibrils reaches 220 nm (figure 2b,c). Finally, the hierarchical helices with mean diameter of approximately 260 nm and length of several to tens of micrometres are obtained.

Similar to the previously synthesized Ag-GSH BCP hydrogel [22], it is found that the Ag-GSH helical nanofibres also show some solubility in water, which is unfavourable for further use in biological systems. Thus, in order to enhance their stability in water, Ca$^{2+}$ ions are introduced into the suspension containing the Ag-GSH BCP helical nanofibres to make them cross-linked. Figure 1c,d shows the transmission electron microscopy (TEM) images of the Ag-GSH BCP helical nanofibres cross-linked with Ca$^{2+}$ ions (denoted as Ca-fibres) at different magnifications. Evidently, after cross-linking, the morphology and chirality of the helical nanofibres are maintained.

Control over the assembly process is crucial to construction of BCPs with well-defined structures. In this study, we manipulate the assembly process by changing the volume ratio between DMSO and water, the Ag/GSH molar ratio and the solvent. The morphology of Ag-GSH BCP prepared at different volume ratio of DMSO to water is shown in the electronic supplementary material, figure S4. When the ratio between DMSO and water is larger than 4/3, a precipitate with spherical morphology is generated immediately after the addition of DMSO. Fast precipitation with a poor solvent has been used in the synthesis of amorphous infinite CPs [7], and powder X-ray diffraction (PXRD) patterns show that the precipitate in this work is also a CP with very low crystallinity (see electronic supplementary material, figure S5). If the ratio between DMSO and water is altered to 3/3, then a mixture of micrometre spheres and untwisted fibres is
Figure 2. Evolution process of the Ag-GSH helical fibres monitored by SEM. (a) Non-helical nanofibrils with diameters of 52 ± 8 nm formed after 12 h. (b) Non-helical nanofibres with diameters of 137 ± 18 nm formed after 24 h. (c) Coexistence of helical and non-helical nanofibres after 48 h. (d) Helical nanofibres with mean diameter of approximately 260 nm after 96 h growth.

obtained. Helical fibres are achieved only when the ratio between DMSO and water is 2/3 or 1.5/3 after 96 h of incubation at 37°C. When the ratio between DMSO and water is further decreased to 1/3, clear solution is obtained without the solid products, and it is changed into a gel after placing at room temperature for several hours. Apart from the volume ratio between DMSO and water, both the Ag/GSH molar ratio and the solvent can also influence the self-assembly process and the final products markedly. For example, it is found that at pH 6.0 and Ag/GSH molar ratio of 1/1, interwoven non-helical belt-like fibres are obtained (see electronic supplementary material, figure S6); similarly, introduction of other solvents such as acetone, ethanol, isopropanol and methanol into the reaction system to replace DMSO as the poor solvent results in the formation of Ag-GSH BCPs with non-helical structures (electronic supplementary material, figure S7). The above results demonstrate that the controlled assembly is essential for formation of the Ag-GSH helical nanofibres.

(b) Ag-GSH helical nanofibres: composition and structure

The composition of the Ag-GSH BCP helical nanofibres before and after cross-linking is investigated in detail. Firstly, both of them are characterized by Fourier transform infrared (FT-IR) spectroscopy. Figure 3 shows the FT-IR spectra of pure GSH molecules, as well as Ag-GSH helical nanofibres before and after cross-linking. One can see that the −SH stretching peak at 2525 cm⁻¹ disappears in the spectra of the Ag-GSH BCP helical nanofibres regardless of whether they are cross-linked or not, indicating that both the Ag-GSH BCP helical nanofibres before and after cross-linking are formed through Ag−S coordination bonds. In addition, the peak at 1713 cm⁻¹ assigned to >C=O stretching vibration of the −COOH group of glycine residue [23] also disappears in the helical nanofibres, demonstrating that both carboxyl groups of GSH are dissociated. Interestingly, in the FT-IR spectrum of the uncross-linked Ag-GSH helical nanofibres, there is a distinct peak at 953 cm⁻¹ attributed to S=O stretching of DMSO molecules. Previous study revealed that DMSO could coordinate with metal ions through either oxygen or sulfur atoms, resulting in a shift from the original S=O stretching frequency at 953 cm⁻¹ (oxygen
Figure 3. FT-IR spectra of (a) GSH, (b) Ag-GSH fibres and (c) Ca-fibres.

Table 1. Relative atomic ratios of N, C, H and S in GSH, Ag-GSH fibres and Ca-fibres obtained from elemental analysis.

<table>
<thead>
<tr>
<th></th>
<th>N</th>
<th>C</th>
<th>H</th>
<th>S</th>
</tr>
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<tbody>
<tr>
<td>Ag-GSH fibres</td>
<td>2.49</td>
<td>9.66</td>
<td>16.51</td>
<td>1</td>
</tr>
<tr>
<td>Ca-fibres</td>
<td>2.86</td>
<td>10.83</td>
<td>18.54</td>
<td>1</td>
</tr>
<tr>
<td>GSH</td>
<td>3</td>
<td>10</td>
<td>17</td>
<td>1</td>
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Coordination decreases the S=O stretching vibration frequency, whereas sulfur coordination follows the opposite tendency) [24]. Nevertheless, the peak at 953 cm\(^{-1}\) demonstrates that DMSO molecules remain free in the helical nanofibres. However, after the Ag-GSH BCP helical nanofibres are cross-linked by Ca\(^{2+}\) ions, the peak at 953 cm\(^{-1}\) disappears, suggesting that free DMSO molecules are removed after Ca\(^{2+}\) cross-linking. Elemental analysis and inductively coupled plasma atomic emission spectrophotometry (ICP-AES) results further confirm this conclusion. It is obvious that the atomic ratio of N, C, H and S in the nanofibres after Ca\(^{2+}\) cross-linking (Ca-fibres) is very close to that in pure GSH molecules (table 1). As a comparison, the N/S atomic ratio in the nanofibres before cross-linking (Ag-GSH fibres) is considerably smaller than that in Ca-fibres, implying the existence of additional S source assigned to free DMSO molecules. The S/Ag atomic ratios obtained from ICP-AES are decreased from 1.339 to 0.867 after cross-linking, also demonstrating release of DMSO molecules (see electronic supplementary material, table S1).

The above discussion reveals that DMSO is not coordinated with Ag\(^{+}\) ions in the BCP fibres, but its role in the formation of Ag-GSH fibres is still not clear. Thus, PXRD is adopted to analyse the crystal structure of Ag-GSH fibres and Ca-fibres (figure 4). There are five diffraction peaks to be distinguished from 5° to 20°, suggesting a layered structure of the fibres. The corresponding d spacings of these peaks are summarized in electronic supplementary material, table S2. The d spacings corresponding to 2θ of 5.31°, 10.65° and 16.04° for the Ag-GSH helical nanofibres are 1.666, 0.831 and 0.553 nm, respectively, which are attributed to successive orders of diffraction (0k0) from the layers (figure 4). After cross-linking, all of these diffraction peaks shift to higher angles, which indicate that d spacings of Ca-fibres are smaller than those of Ag-GSH fibres. The layer spacing decreases to 1.592 nm after Ca\(^{2+}\) cross-linking, which approaches two times the length of GSH molecules in T-shaped conformation (the height of T-shaped GSH molecule is 0.759 nm, and 0.759 \(\times\) 2 = 1.518 nm) [25]. In addition, the diffraction peaks at 2θ of 9.26° and
14.16° for Ag-GSH fibres and 9.61° and 14.69° for Ca-fibres might be assigned to intralayer reflections [12,22,26,27]. From the spectroscopy, element analysis and diffraction results, we propose that the Ag\(^{+}\) ions coordinate with GSH molecules via Ag–S bonds to form two-dimensional layered structures [12,22,26,27]. GSH molecules extend from both sides of the layers in a T-shaped conformation and DMSO molecules are located between the layers (figure 5). During the cross-linking process, Ca\(^{2+}\) ions replace DMSO and give rise to decrease of d spacing. DMSO not only provides the poor solvent condition but also acts as a component between the layers to promote formation of the helices.

(c) Ag-GSH helical nanofibres: chirality and plasmon-induced optical activity

Thanks to the chiral nature of L-GSH molecules, the Ag-GSH BCP fibres are expected to exhibit certain optical activity. Simple mixture of Ag\(^{+}\) ions and L-GSH molecules in the solution shows
no strong circular dichroism (CD) in the region more than 300 nm. By contrast, the CD spectrum of the prepared Ag-GSH fibres exhibits a pair of sharp peaks centred at 343 and 364 nm after 96 h of incubation at 37°C (see electronic supplementary material, figure S8). Consistent with our previous study [12], the bisignate Cotton effects at 343 and 364 nm should arise from the coupling low-energy ligand-to-metal charge-transfer bands in the extended coordination frameworks. After cross-linking with Ca$^{2+}$ ions, the characteristic CD spectrum of the helical nanofibres remains almost unchanged (solid curve in figure 6c), implying that the extended coordination framework in Ag-GSH fibres is unaltered after cross-linking with Ca$^{2+}$ ions.

The prepared Ca-fibres are found to be well dispersed in water, and this observation is in agreement with experimental measurement that Ca-fibres are negatively charged with a zeta potential of $-30.0 \text{ mV}$ (see electronic supplementary material, figure S9). The negative surface charge should originate from the surface carboxylate groups that are not coordinated with Ca$^{2+}$ ions, which is supported by the detected residual Na$^+$ ions shown in ICP-AES measurement (see electronic supplementary material, table S1). Because the Ca-fibres exhibit well-defined helical structure and keep well dispersed in water, they can be used as chiral scaffold for organization of nanoparticles in a three-dimensional chiral manner. Among all inorganic nanoparticles, noble metal nanoparticles especially gold and silver are of special research interest owing to their strong LSPR effect. Plasmonic nanoarchitectures have been constructed by bottom-up self-assembly and/or top-down lithography, showing a number of applications in diagnostics,
energy-harvesting, nanophotonic circuits and so on [28]. Recent studies including our group’s results have found that when chiral molecules or their assemblies are in proximity to noble metal nanoparticles, plasmon-induced CD in the visible or near-infrared region will appear owing to transportation of chirality from chiral molecules or templates to nanoparticles [29–31]. It should be noted that there have been some reports on the optical activity of gold or silver nanospheres or nanorods that are adsorbed on chiral molecular assemblies, such as DNA [32,33], peptides [34] or artificial chiral molecules [35]. However, the plasmon-induced CD property of the composites containing noble metal nanoparticles and helical nanofibres of CPs or BCPs has not yet been investigated.

In this study, positively charged and cetyltrimethylammonium bromide (CTAB)-coated gold nanorods with longitudinal LSPR peak at 643 nm (see electronic supplementary material, figure S10) are adsorbed onto the helical Ca-fibres via electrostatic interaction. Figure 6a, b shows the TEM images of the Ca-fibre/gold nanorod composites, in which gold nanorods are observed to be distributed on the helical fibre surface randomly. UV–visible absorption spectra further show that besides preservation of the absorbance peak of Ag-GSH fibres at 359 nm, the characteristic resonance bands of transverse (approx. 520 nm) and longitudinal (approx. 640 nm) LSPR modes of gold nanorods appear for the Ca-fibre/gold nanorod composites (dashed curve in figure 6d). The CD spectrum of the composites presents a bisignate Cotton effect at 554 and 710 nm, which is consistent with the absorbance peak of the longitudinal LSPR (dashed curve in the inset in figure 6c). We also note that the plasmon-induced CD is not very strong compared with the CD signal of original Ca-fibres (figure 6c). The reason may result from random arrangement of the gold nanorods on Ca-fibres, which are still far away from the optimization of the optical activity with the gold nanorods of chiral ordering. Nevertheless, this type of chiroptical materials may provide a new route for use in nonlinear optics [36], biosensing [37,38] and negative refraction [39].

In conclusion, the hierarchical helical nanofibres of Ag-GSH BCP are constructed by the controlled self-assembly of Ag-GSH complex in DMSO/water mixed solvent. Characterization of the intermediate process discloses that hierarchical helical structures are formed by entangling and twisting of smaller fibre units. In addition, DMSO molecules are found to not only act as the poor solvent that trigger the self-assembly process but also a component between GSH molecules to promote formation of the helices. DMSO molecules are easily replaced by Ca$^{2+}$ ions, and thus the cross-linked fibres are produced. These cross-linked fibres are well dispersed in aqueous solution with negative surface charges. As a result, positively charged gold nanorods could be adsorbed onto the surface of the helical nanofibres to construct composites based on electrostatic attractions. A distinct plasmon-induced CD feature appears in the longitudinal LSPR region of gold nanorods for the composites of the helical fibres and gold nanorods. It is expected that this type of chiroptical metamaterials will have potential applications in nonlinear optics, negative refraction and biosensing.

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References


