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Effect of Al(III) and Curcumin on Silk Fibroin Conformation and Aggregation Morphology

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Abstract

Misfolding or β-sheet nano-fibrillation of specific proteins is considered to be an underlying pathogenic mechanism of neurodegenerative diseases. It's found previously that Al(III) can affect the β-sheet nano-fibrillation and deposit of neurodegenerative diseases-related proteins, and curcumin can interact with metal ions and those proteins. In this work, silk fibroin (SF) was used as a model fibrillation protein for investigation of the influence of Al(III) and curcumin on silk fibroin conformation transition. The effects of Al(III) and curcumin on silk fibroin were investigated by circular dichroism (CD), thioflavin-T (ThT) fluorescence, 1-anilino-8-naphthalene sulfonate (ANS) fluorescence, turbidity assays, atomic force microscope (AFM) and Fourier transform infrared (FTIR). It is demonstrated that Al(III) can bind with specific amino acids residues of silk fibroin, and then accelerate the formation of intermediates and further the formation of nano-fibrils. The concentration of Al(III) is an important factor that influence the folding speed of silk fibroin. Furthermore, curcumin can not only restrain the conformation transition of silk fibroin, but also reverse the conformation transition of SF and Al(III)-induced SF from insoluble β-sheet to soluble random coil. Curcumin may prevent the neurodegenerative-related proteins from nano-fibrillation and aggregation.

Keywords: neurodegenerative diseases, silk fibroin, nano-fibrillation, Al(III), curcumin

Introduction

Neurodegenerative diseases including Alzhermer's disease (AD), prion disease and Parkinson's disease have threaten human health for years.[1-4] One of the pathogens involves the abnormal aggregation of neurodegenerative-related proteins such as amyloid β (Aβ) peptide.[5-7] The nano-fibrillation and aggregation of Aβ40 and Aβ42 which are derived from proteolytic cleavage of amyloid precursor protein in senile plaques and neuritic plaques are main characteristics of Alzheimer's disease pathology.[8-10] It's found that the typical hydrophobic sequence, VGGAVVAGV, in Aβ peptide is similar to the peptide segment, GAGVGAGYG, which is abundant in the silk fibroin (SF) of *Bombyx mori* silkworm,[11,12] and the mechanism of nano-fibrillation is also similar between two proteins.[13] Accordingly, we used SF, an easily available protein, as a model fibrillation protein to simulate the aggregation process of Aβ. SF has two types of conformers: Silk I (random coil and helix-like forms) and Silk II (β-sheet and β-sheet-like forms).[14,15] The morphology of Silk I solid is amorphous while that of silk II solid is crystalline in β-sheet fibrils. It has been reported that the process of protein self-assembly into nano-fibrils was stabilized by cross-β interactions.[16] Previously, we demonstrated that K^+, Ca^{2+}, Cu^{2+} and Zn^{2+} ions could affect the secondary structures of the regenerated silk fibroin and accelerate the conformation transition from silk I to Silk II at certain concentrations.[17-22]

Al(III), enriched in senile plaques, is related with the fibrillation, aggregation and toxicity of Aβ.[23,24] However, the detailed mechanism of Aβ nano-fibril formation is still unclear. In fact, the research about spinning mechanism of silkworms shows that

the process of forming SF fibrils has similar dynamic behavior to that of denaturizing Aβ.[13] On the basis of the resemblance between Aβ and SF, we used SF as a model protein to study its interaction with Al(III).

Previous report revealed that chelators such as desferrioxamine and clioquinol have anti-AD ability.[25] In addition, it was found that the gel of SF was caused by cross-linking via metal ions present in the solution; while the solution could be converted from gel to sol state by EDTA.[26] Therefore, this work tried to find a physiological nontoxic substance capable of chelating the metal ions efficiently, and stabilizing the fibroin in solution at state of random-coil conformation, or even reversing the preformed β-sheet conformers into random-coil ones.

Curcumin, a planar biphenolic yellow pigment (Fig. 1) found in turmeric commonly used in India and other Asian countries, is reported to have some therapeutic effects on AD.[27,28] The ability of crossing blood brain barrier and non-toxicity makes curcumin more appealing than many other molecules.[29,30] In addition, Yang et al[31] suggested that curcumin could bind with amyloid, and then inhibit Aβ aggregation. Garcia-Alloza[32] reported that curcumin could disrupt the existing plaques, and partially restore the distorted neurites in Alzheimer model mouse. Baum etal[25] also suggested that curcumin could interact with copper and iron, reducing amyloid aggregation or oxidative neurotoxicity. Although the research of curcumin on Aβ is underway, there is few reports about the interaction of curcumin with Al(III).

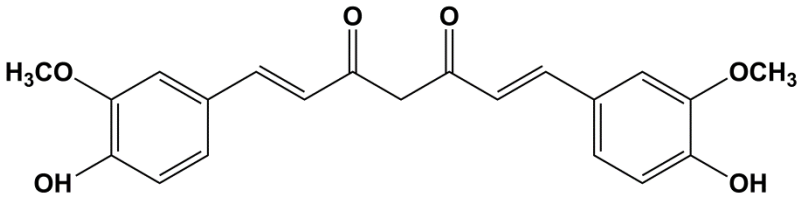


Fig. 1 Molecular structure of curcumin.

In our previous work,[33] Al(III)/curcumin/SF samples in solid state were studied. While, the drying process involved the concentration change which also influenced the SF conformation transition and the formation of aggregations. In this work, Al(III)/SF samples in solution state were studied. We investigated the chelating sites of Al(III) in SF, and the effects of Al(III) on the conformational transition and fibrillation of SF. Furthermore, the research of SF/Al(III)/curcumin mixture solution figured out the effect of curcumin on SF and Al(III)/SF system. This work would shed some light on the way to prevent and cure AD.

2. Materials and Methods

2.1 Materials

The cocoon of silkworm *Bombyx mori* was purchased from Yuxing Textile Factory in Tongxiang, Zhejiang province, China. Curcumin was purchased from Alfa Aesar (Ward Hill, MA). 8-anilino-1-naphthalenesulfonate (ANS), thioflavin T (ThT) and tris-hydroxymethy amino-methane (Tris) were purchased from Sigma and Aldrich, USA. Lithium bromide (LiBr), silver nitrate ($AgNO_3$), sodium carbonate (Na_2CO_3), hydrochloric acid (HCl) and aluminum chloride ($AlCl_3$) were purchased from Sinopharm, China.

2.2 Preparation of SF solution

The raw silk fibers from *Bomyx mori* cocoons were degummed twice by boiling water for 40 min each time in a 0.5 wt% Na_2CO_3 solution to remove sericin, and then the degummed silk fibers were thoroughly rinsed with ultra-pure deionized water (resistivity ~ 18.2 MΩ•cm) and dried overnight at 60°C in a drying oven. 6 g degummed silk fibers were dissolved in 100 mL, 9.3 M LiBr aqueous solution. After the silk fibers were completely dissolved, the solution was filtered and dialyzed against ultra-pure deionized water with a 14000 g mol^{-1} dialysis tube to remove LiBr which was probed by 0.1 M $AgNO_3$ aqueous solution. The final concentration of aqueous SF solution was about 1.5 wt%.

2.3 Preparation of Al(III)/SF solutions and films

SF solution (10 mg mL^{-1}) was mixed with different concentration (0, 5, 10 mM) Al(III) solution to get 6 mL mixture solution. The resulted solutions were cast on 30 × 30 cm

polyester dishes, and then dried for 3 days in the fume hood, leading to the films containing 60 mg SF each one. The drying process was to mimic the spinning process of silkworm from aqueous solution to insoluble fibers.

2.4 Preparation of mixture samples of SF, Al(III) and curcumin

For study of Al(III) interaction with SF, SF solutions were mixed with various volumes of 2 mM $AlCl_3$ aqueous solution and then diluted by Tris-HCl aqueous solution (20 mM, pH = 7.4) to 26 ml at SF concentration of 0.5 mg/mL, and Al(III) concentration of 0, 10, 15, 20, 40, 50, 60, 80, 100 μM, respectively. Curcumin/SF solutions were prepared with 15 μM curcumin and 0.5 mg/mL SF, and Al(III)/cucumin/SF solution was prepared with 15 μM $AlCl_3$, 15 μM curcumin and 0.5 mg/mL SF. For study the morphology of SF aggregation, 0.5 mg/mL SF was incubated for 10 days to produce precipitates, and then diluted by ultrapure water and then ultrasound.

2.5 Circular dichroism

Circular dichroism (CD) spectrum of SF was recorded by Jasco J-715 spectropolarimeter with a quartz cell of 1 mm path length. All CD spectra were recorded by five scans at a speed of 100 nm/min with a response time of 0.5 s. The range of scan was from 190 to 250 nm with 15 mL/min nitrogen flow during the process.

2.6 Fluorescence spectroscopy

Fluorescence spectrum (FLS) was recorded by a FLS-920 fluorescence spectrophotometer (Edinburgh Instrument, U.K.) with a 1.0 cm path length quartz cell.

For fluorescence measurement, the interaction of 30 μM ANS with SF was monitored by fluorescence emission at 500 nm (λ_{ex} = 360 nm), and that of 20 μM ThT with SF by emission at 485 nm (λ_{ex} = 450 nm).

2.7 Turbidity assay

Relative turbidity of turbid SF solution was recorded by UV-Vis scattering at λ = 400 nm. UV-Vis scattering measurement was performed by a Perkin Elemer Lambda 35 UV/Vis spectrometer.

2.8 Atomic force microscope images

5 μL of Al(III)/cucumin/SF mixture sample was freshly collected and swiftly diluted to 5 μg/mL solution with water. 10 μL of diluted solution was mounted onto the freshly cleaved mica for 5 min, gently rinsed with water, and dried in vacuum overnight. Images were acquired under atmosphere by silicon probe in tapping mode packaged in multimode 8 system (Bruker, Germany).

2.9 Attenuated total refection-Fourier transform infrared spectroscopy

Attenuated total refection-Fourier transform infrared spectroscopy (ATR-FTIR) measurements were performed by a Nicolet Nexus 470 FTIR spectrometer equipped with ZnSe crystal as window material and Omin sampling accessories.

3. Results

3.1 Conformation transition of SF induced by Al(III) in solution state

To study the effects of Al(III) on SF conformation transition, the conformation of SF in solution were detected by CD, fluorescence and UV-Vis scattering.

The secondary structure of SF has special ellipticity bands between 178 - 250 nm in CD. Random-coil conformation has negative strong band at 195 nm; β-sheet structure has negative broad band at 217 nm and positive strong band at 197 nm.[34, 35]

ThT is a fluorescent dye that can selectively associate with β-sheet or the aggregated forms of protein, resulting in the fluorescence enhancement,[36] therefore generally used to probe the hydrophobic β-sheet conformation.

In addition, ANS usually also interacts with hydrophobic blocks of partially folded proteins and oligomers because of its hydrophobicity, resulting in the enhancement and blue shift of ANS fluorescence,[37, 38] therefore, ANS is used to probe the intermediates of folded proteins and oligomers.

The turbidity of Al(III)/SF solution was monitored by UV-Vis scattering at 400 nm. The increase of UV-Vis scattering intensity implies the aggregation of SF.

pH is an important factor to impact the conformation transition of SF.[17] To explain the effect of Al(III) on SF clearly, it should be excluded. pH of the low concentration of Al(III) solution was kept from 7.33 to 7.27 by Tris-HCl buffer.

Fig. 2A shows the conformation transition of SF detected by CD at different incubation time with Al(III). It is found that the amount of β-sheet conformers of SF

was increased during incubation, and the amount is higher in Al(III)/SF solution than that in SF solution, based on the ellipticity at 217 nm. Fig. 2B shows the ThT fluorescence intensity in SF in absence and presence of Al(III). After Al(III)/SF solution was incubated for a given time, ThT was added into the solution. The fluorescence curve was fitted on sigmoidal model, showing a low plateau phase at beginning, called as a lag phase, and then rapid increase, and finally a high plateau phase after 26 h of incubation in both absence and presence of Al(III). The results indicates that Al(III) accelerated the formation of β-sheet conformer. Fig. 2C shows the ANS fluorescence impacted by the interaction of SF with different Al(III) concentration after the solution was incubated for 10 h. It is found that the intensity of ANS fluorescent increased with Al(III) concentration increased, indicating that more intermediates of β-sheet SF were formed at higher Al(III) concentration. Fig. 2D shows the ThT fluorescent of Al(III)/SF solutions after incubation for 10 h. Fig. 2E shows the turbidity of SF solution with different Al(III) concentrations. The trend of Fig. 2E is similar to that of Fig. 2D, indicating that the formation of β-sheet conformers and their precipitates depended on the Al(III) concentration.

Above results demonstrates that Al(III) can promote the formation of β-sheet conformers, leading to the fibrillation and aggregation of SF.

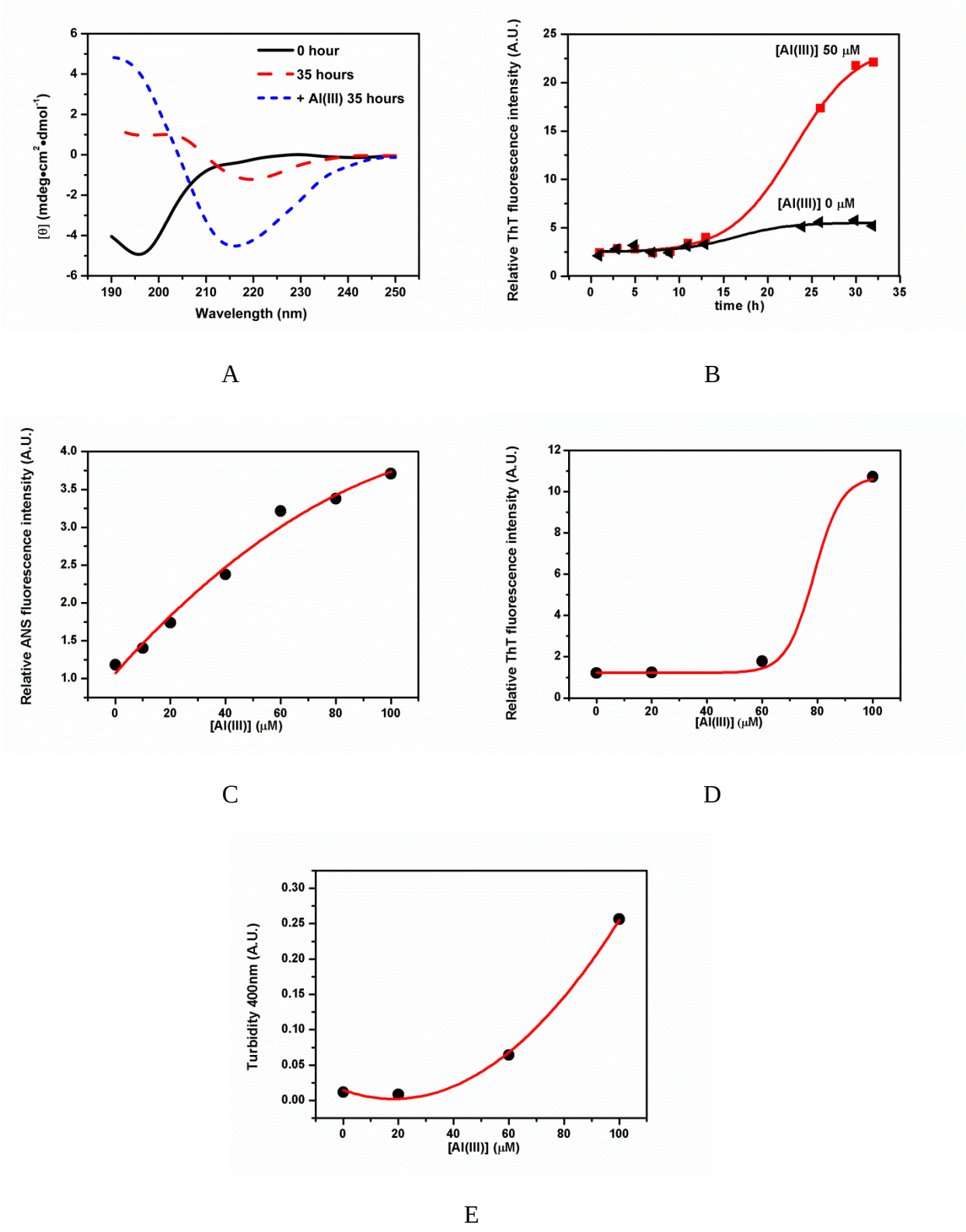


Fig. 2 (A) CD spectra of SF incubated for different time in the absence and presence of 50 μM Al(III). Solid (in black), dash (in red) and dot (in blue) curves represent SF solution after

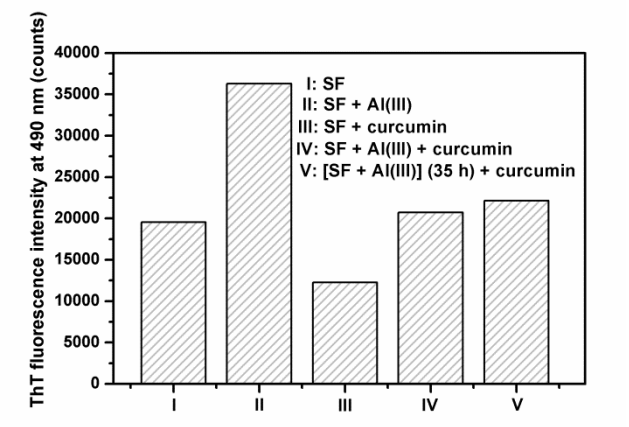
incubated for 0, 35 h and 35 h with Al(III), respectively. (B) Fibrillation kinetics of silk fibroin on Al(III) treatment were monitored by ThT fluorescence at 485 nm for 35 hours. (C) ANS fluorescence at 500 nm after silk fibroin incubated for 10 hours in the presence of Al(III) with various concentrations. (D) ThT fluorescence at 485 nm after silk fibroin incubated for 10 hours in the presence of Al(III) with various concentrations. (E) The relative turbidity of silk fibroin which was pre-incubated for 35 hours in the presence of Al(III) with various concentrations was detected by UV-Vis scattering at 400 nm.

3.2 Effect of curcumin and Al(III) on secondary structure of SF

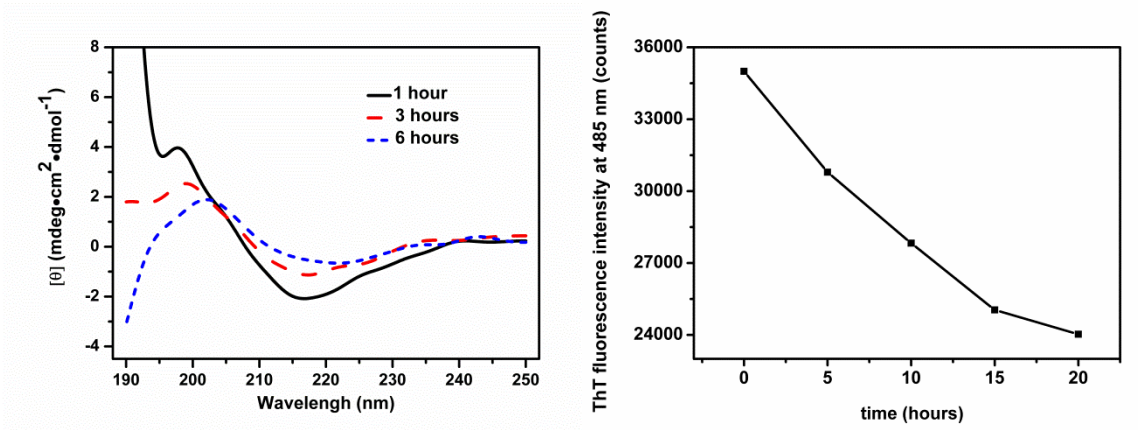
In order to investigate the effects of curcumin, ThT fluorescence in SF, Al(III)/SF, curcumin/SF and Al(III)/curcumin/SF solutions were measured, respectively. Fig. 3A shows that ThT fluorescence intensity is in order as Al(III)/SF > SF > curcumin/SF. Besides, ThT fluorescence intensity of Al(III)/SF solution was higher than that of Al(III)/curcumin/SF (where Al(III) to curcumin ratio of 1 : 1) mixture solution incubated for 35 h. The results indicate that Al(III) could accelerate the conformation transition and fibrillation of SF, and curcumin could inhibit Al(III)-induced SF conformation transition.

Fig. 3B shows CD spectra of Al(III)/SF solutions which were pre-incubated for 35 hours, and then curcumin was added for additional 1, 3, 6 h incubation, respectively. It is found that the negative peak at 217 nm became weak, which indicates that the conformers of β-sheet were decreased gradually. That is, curcurmin could remold the preformed β-sheet into random coil. Fig. 3C shows ThT

fluorescence in Al(III)/SF solutions which were pre-incubated for 35 hours, and then curcumin was added for additional 5, 10, 15, 20 h incubation. ThT fluorescence intensity decreased during incubation, indicating that curcumin could disaggregate the preformed SF fibrils, which is the same as the results from CD measurement.



A



B C

Fig. 3 (A) ThT fluorescence intensity at 485 nm for samples as silk fibroin incubated for 35 hours (I: SF), in the presence of 15 μM Al(III) (II: SF + Al(III)), 15 μM curcumin (III: SF + curcumin), and in both of them present (IV: SF + Al(III) + curcumin). Sample V ([SF+Al(III)] (35 h) +curcumin) is the solution where 15 μM curcumin was added after SF/Al(III) solution was incubated for 35 h. (B) CD spectra where SF was pre-incubated with 15 μM Al(III) for 35 h and then 15 μM curcumin

was added for further incubation of 1, 3, 6 hours. (C) ThT fluorescences at 485 nm where SF was pre-incubated with 15 μM Al(III) for 35 h, and then 15 μM curcumin was added for further incubation of 5, 10,15, 20 hours.

3.3 Morphologies of aggregates detected by AFM

Fig. 4 shows the AFM images of serious SF samples. Fig. 4A shows the nano-fibrils in height about 2.5 nm where SF precipitates were formed by evaporating water in SF solution. This process is similar to that of silkworm spinning along with water removed from the gland and protein concentration increased. Fig. 4B – 4E are images for SF (B), Al(III)/SF (C), curcumin/SF (D) and Al(III)/curcumin/SF (E) samples which were incubated for 35 h, where the heights of particles are about 4.5 (B), 14.0 (C), 3.0 (D), 6.5 (E) nm, respectively. Fig. 4F-1 – 4F-4 are images of Al(III)/SF samples pre-incubated for 35 h and then treated by curcumin for another 5 h (F-1), 10 h (F-2), 15 (F-3), and 20 h (F-4) incubation, where the heights of particles are about 6.5, 6.5, 3.5, 4.5 nm, respectively.

The sizes of Al(III)/SF particles (Fig. 4C) are larger than that of SF (Fig. 4B), which demonstrates that Al(III) promoted the SF aggregation. Comparison of Fig. 4B and 4C with Fig. 4D and 4E, it is found that curcumin inhibited the SF and Al(III)-induced SF aggregation. Fig. 4F-1 – 4F-3 show the process of nano-fibrils disappearing gradually to the oligomers when curcumin was added, and 20 hours later (4F-4), the oligomers become lager, and the heights become higher, which demonstrated that oligomers formed the amorphous aggregates.

The morphology of SF precipitates in Fig. 4A is different from that in other Fig. 4's, indicating that nano-fibril formation may require higher concentration of protein than particle formation. The environment interference such as Al(III) and curcumin presence in the protein influences the formation of nano-fibrils.

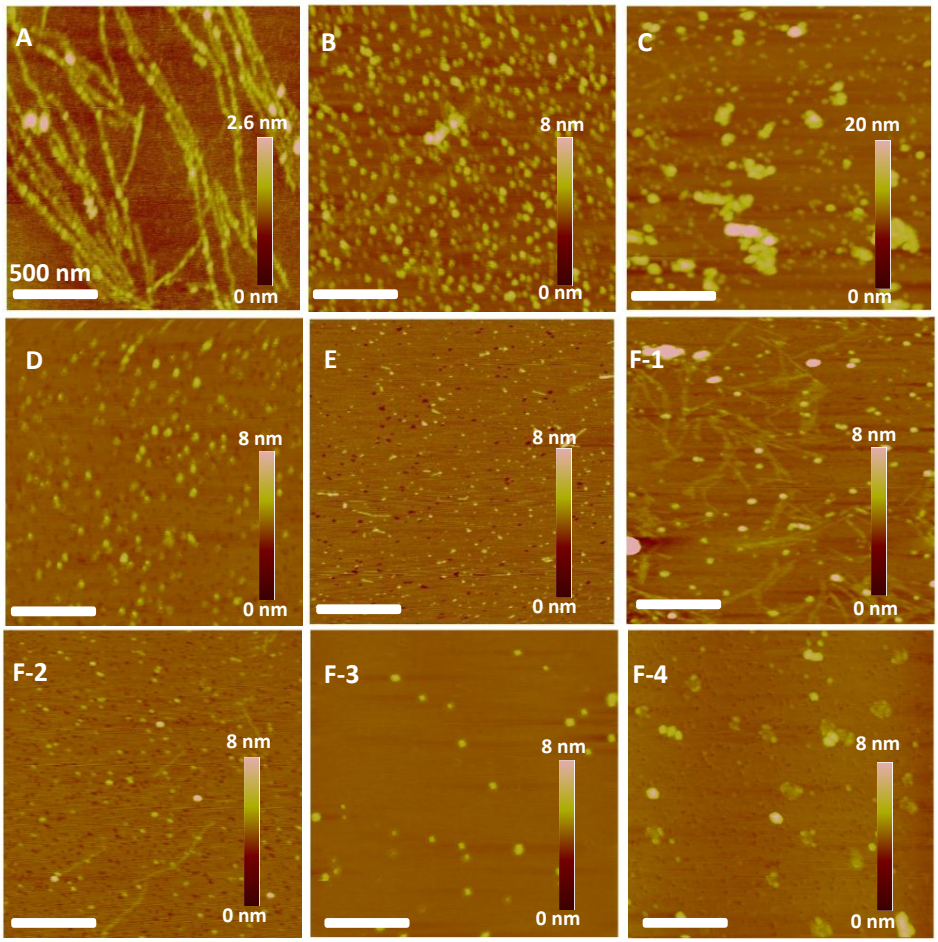


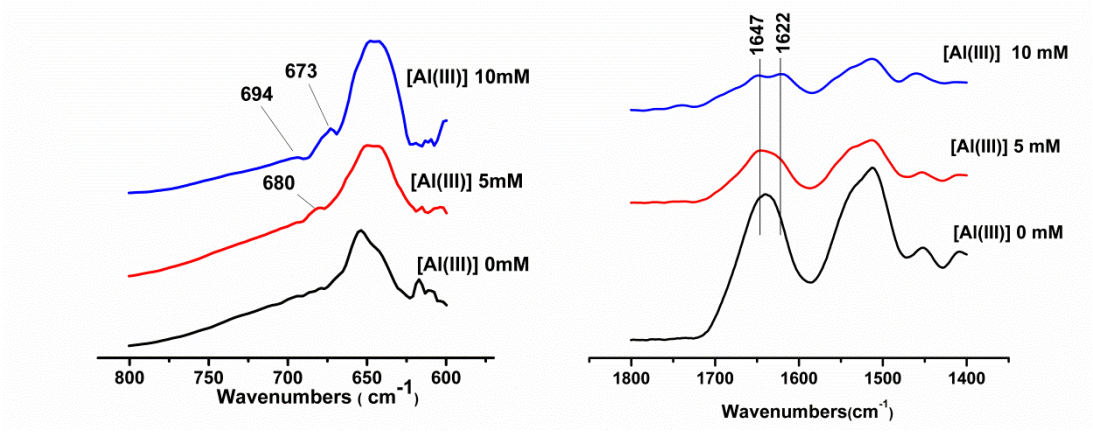
Fig. 4 AFM images of SF precipitates (A); SF incubated for 35 hours (B); SF incubated for 35 hours in the presence of Al(III) (C); SF incubated for 35 hours in the presence of curcumin (D); SF incubated for 35 hours in the presence of Al(III)/curcumin (E); SF and Al(III) co-incubated for 35 hours and curcumin was added for additional 5 (F-1), 10 (F-2), 15 (F-3), and 20 hours (F-4), respectively.

3.4 Interaction of Al(III) with SF on FTIR study

For viewing insight into the interaction between Al(III) and SF on molecular level, FTIR spectroscopy was investigated. Fig. 5A shows that SF films containing 5 mM Al(III) appeared new broad peak near 680 cm^{-1}, compared with the pure SF film; while when the concentration of Al(III) was increased to 10 mM, there existed two new sharp peaks at 694 cm^{-1} and 673 cm^{-1} clearly. It was reported that the stretching vibrations of Al-N bonds appear at 621, 672 cm^{-1}, and that of Al-O bonds appear at 500 - 750 cm^{-1}.[39] Therefore, we speculate that the peak at 680 or 694 and 673 cm^{-1} might result from stretching vibration of octahedral Al-O and Al-N bond, respectively.[40]

In addition, infrared absorption frequency of amide groups in protein is quite sensitive to the secondary structure. Infrared spectral region within 1700 - 1600 cm^{-1}, namely amide I, shows high intensity and little interference from other group vibrations, compared with amide II (1600 - 1500 cm^{-1}) and amide III (1330 - 1220 cm^{-1}), thus is widely used to analyze the conformation change of protein. In amide I band, the adsorption peaks are generally assigned as: 1653 ± 4 cm^{-1} to helix, 1645 ± 4 cm^{-1} to random coil, 1625 ± 5 cm^{-1} and 1675 ± 5 cm^{-1} to β-sheet, 1663 ± 4 cm^{-1} to β-turn.[41] Fig. 5B shows the spectra of SF incubated with Al(III) at various concentrations. It is found that the absorption band at 1625 cm^{-1} corresponding to antiparallel β-sheet increased, and that at 1647 cm^{-1} corresponding to random coil decreased with concentration of Al(III) increased. The results reveal that Al(III) can effect with SF and result in the transition from random coil to β-sheet, which

demonstrate the results from CD in Fig. 2.



A B

Fig. 5 FT-IR spectra of silk fibroin in the presence of Al(III) at various concentrations. (A) FT-IR spectra of SF in fingerprint region. (B) FT-IR spectra of SF in amide I region.

4. Discussions

In combination with the results from CD, ANS-FLS, ThT-FLS, UV-Vis scattering, AFM, as well as ATR-FTIR, the work provides an insight into the role of Al(III), curcumin affecting the conformation transition of SF.

Interaction between Al(III) and SF. FTIR results show that Al(III) can bind to oxygen atoms (absorption peak at 680 and 694 cm^{-1}) and nitrogen atoms (absorption peak at 673 cm^{-1}) (Fig. 5A). There are relatively high contents of serine (Ser, 10.8%), tyrosine (Tyr, 4.9%) and aspartate (Asp, 1.5%) in SF.[42] With –OH groups in the side chains of Ser and Tyr, and –COO in Asp, these amino acid residues are the right sites for Al(III) and other metallic ions such as Ca^{2+} or Mg^{2+} binding.[43,44,45] In addition, Lys, Arg and His have nitrogen atoms at the side chain. Therefore, it is supposed that the

bonded nitrogen atoms might from these amino acids.

Effect of Al(III) on SF conformation transition and fibrillation. The work shows that Al(III) can promote SF conformation transition. The process of SF aggregation undergoes the "nucleation-dependent polymerization", and Al(III) ions accelerate the process (Fig. 2). SF gradually changed its conformation from random coil to β-sheet as detected by CD (Fig. 2A) as well as ThT fluorescence (Fig. 2B) where ThT selectively associated with β-sheet conformation of protein, and then formed partially the β-sheet folded proteins or folded oligomers, namely the "nucleus" or intermediates which were verified by ANS fluorescence where ANS interacted with hydrophobic blocks of β-sheet proteins because of its hydrophobicity (Fig. 2C). While Al(III) ions accelerate the formation of β-sheet SF, which was demonstrated by ThT fluorescence (Fig. 2D). The resulting aggregates were detected by UV-Vis scattering (Fig. 2E) as well as AFM images (Fig. 4). During the process of fibrillation and aggregation of SF, Al(III) promoted and accelerated the protein folding. It has been reported that the heavy chain (H-chain) silk fibroins contain Asp and Glu at the N-terminus and C-terminus,[11,46] and their -COO at the side chains, which allows the terminus highly hydrophilic. In addition, there are some hydrophilic spacers, GTGSSGFGPYVA (N/H), GGYSGYEYAWSSESDFGT, locating between the long hydrophobic blocks in the protein central region.[11] H-chain fibroins have a pI (isoelectric point) of 4.2, implying that at near neutral pH, the predominant negative charges in SF would prevent intra- and inter- molecular hydrophobic interaction by their strong static electric repulsion, which keeps the hydrophobic blocks from

approaching and aggregating.[26] Interestingly, of all those amino acids binding Al(III), acidic Asp predominates in the hydrophilic N-terminus of H-chain fibroin, and Ser and Tyr are abundant in the hydrophobic central region. Therefore in a neutral solution with pH higher than pI of 4.2, the charges of amino acids show negative, allowing Al(III) binding to these amino residues easily, and neutralizing the negative charges in SF effectively, and then reducing the static electric repulsion among the hydrophobic blocks, leading to the protein approaching each other easily,[47,48] and resulting in the intra- and inter- molecular hydrogen bonding between those hydrophobic blocks, and promoting the aggregation of SF. Moreover, there are 17.2% amino acids like Ser, Tyr, Asp and Glu,[42] which is able to bind with Al(III) in SF. 100 μM Al(III) in samples used in the fluorescence and turbidity analysis are half of the maximum concentration for binding those amino acids, far lower than the saturation concentration for binding, thus more Al(III) added would lead to more amino acids bound, and the acceleration of the SF aggregation. Therefore, Al(III) promoted SF oligomers and aggregation concentration-dependently, which were observed by ANS fluorescence (Fig. 2C), ThT fluorescence (Fig. 2D) and turbidity assay (Fig. 2E).

From above discussion, we suggest that Al(III) can accelerate the nucleation and aggregation of SF. Al(III) presented in the brain could cause the damage of the neural system, since the aggregative capacity of Al(III)-protein could bring the dramatically structural changes of the membranes in the early stage of the disease,[49,50] meanwhile, the nano-fibrils and precipitates caused by Al(III) could induce the tangle structure of proteins and worsen the disease. Therefore, the mechanism of the aggregation of

neurodegenerative protein, induced by Al(III), might be similar to that of SF.

Influence of curcumin and Al(III) on SF. It is found that adding curcumin to SF or Al(III)/SF solutions decreased the intensity of ThT fluorescence shown in Fig. 3A, indicating that the β-sheet conformers were decreased, meanwhile, the random coil conformers were increased, as demonstrated by CD spectrum (Fig. 3B). Moreover, ThT fluorescence intensity was decreased (Fig. 3C) and the aggregate sizes were reduced (Fig. 4). Therefore, we suggest that curcumin could disaggregate the preformed β-sheet conformers or nano-fibrils into the random coil conformers.

Curcumin, a planar biphenobic molecular, which is similar to ThT, can bind and insert into the plagues proteins.[31,51] Curcumin may damage the hydrogen bonding between protein chains, and then inhibit the formation of β-sheet conformation, and further the formation of fibrils.[33]

In addition, aromatic rings have been considered playing important role during the process of protein fibrillation.[52-54] Miya et al[54] reported that Phe ring in islet amyloid polypeptide $(IAPP)_{22-27}$, for example, can interact with phenol rings in catechins. Therefore, phenol rings in curcumin were supposed to interact with those amino acids which have aromatic rings as Tyr, Trp. Meanwhile, curcumin has an ability to chelate Al(III), thus inhibiting the process of Al(III)-induced conformation transition of SF from random coil to β-sheet.[55]

Conclusions

The results presented above show that Al(III) could bind to amino acids (Ser, Tyr, Asp,

His) in SF, reduce the static electric repulsion among hydrophobic blocks in intra- and inter- molecular and the energy barrier required for folding and aggregation of SF, thereby accelerate the nucleation and aggregation. Our work also indicates that curcumin could prevent the aggregation of SF, and even disaggregate the preformed SF nano-fibrils by changing the β-sheet conformations into random coil ones. Curcumin might be used as a potential drug to prevent and treat AD.

Acknowledgements

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Conflict of interest

The authors declare that there are no conflicts of interest.

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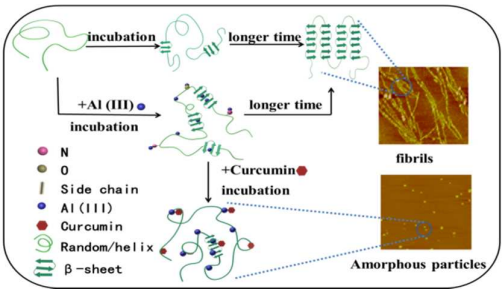
Table of Contents Entry



Al(III) can accelerate the conformation transition of silk fibrion from random coil into β-sheet, and curcumin reverse the transition.