The Structures of Fibril Aggregates of Beta-amyloid Peptide 1-40 upon Addition of Dihexanoylphosphatidylcholine

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ABSTRACT

The amyloid peptide 1-40 forms fibril aggregates having lengths larger than several microns and a diameter around several nanometers. The growth rate and the average length of the fibril can be tuned by adding amphiphilic molecules. In this study, we will show that the addition of dihexanoylphosphatidylcholine (diC_6PC) can effectively reduce the growth rate of the amyloid fibrils and can be used to tune the average length of the amyloid fibrils. The growth process was studied by using AFM and also dynamic light scattering.

Keywords: amyloid peptide, fibril, AFM, dynamic light scattering

1 INTRODUCTION

The amyloid peptides were found to form fibril aggregates in aqueous solutions and the formation of fibril aggregates is thought to be the cause of the Alzheimer's disease [1-2]. It was found that the beta-amyloid 1-42 forms fibril aggregates much faster than the shorter beta-amyloid 1-40 [1]. During the growing process the average length of the fibril aggregates increase with time while the diameter did not vary much. The rate of the fibril growth depends on the concentration, temperature and time of aggregation. Typical diameter of the fibril is in the range of 3 to 8 nm, and the length could reach several microns [2]. The aggregation of the amyloid peptide can be slowed down by adding amphiphilic molecules such as $C_{12}E_6$ at a few mM concentrations [3].

Besides its significance on causing the Alzheimer's disease, the highly stable fibril aggregates of amyloid peptides is an ideal template for growing nanowires. In this study, we will show that the addition of dihexanoylphosphatidylcholine (diC_6PC) can reduce the growth rate of the amyloid fibrils and can be used to tune the average length of the amyloid fibrils. The diC_6PC is a synthetic amphiphilic molecule with a critical micelle concentration (cm) of about 15 mM and they form globular micellar aggregates in aqueous solutions when the concentration is higher than the cmc [4].

2 EXPERIMENTALS

In order to have a better control of the length of the aggregated fibrils, diC_6PC at 1, 2 and 3 mM were added to 0.1 M HCl solutions containing 0.125 mM beta-amyloid 1-40. At these diC_6PC concentrations, the diC_6PC will not form pure diC_6PC micellar aggregates since these concentrations are lower than its cmc. The beta-amyloid 1-40 was purchased from Sigma Co. and the synthetic diC_6PC was purchased from the Avanti Polar Lipids Co. They were used without further purification. A Digital Instruments Dimension 3100 AFM was used to scan the fibril aggregates formed by amyloid peptides. Dynamic light scattering was performed by using the Brookhaven BI-90 goniometer and BI8000AT correlator.

3 RESULTS

As investigated by AFM, Fig. 1 shows the aggregated fibrils without adding the diC_6PC at 21 days after preparing the sample. The fibrils grew to several microns in length. The height (diameter) is about 3 to 8 nm. As a comparison, Fig. 2 shows the sample added with 1 mM diC_6PC at 21 days. Most of the fibrils shown in Fig. 2 have lengths about 1 micron or shorter. The height (diameter) of these fibrils is about 4 nm. Increasing the concentration of diC_6PC to 2 and 3 mM will further reduce the average length of the aggregated fibrils at a similar period of aggregation time. More accurate monitoring the growth of the fibril was carried out by using the dynamic light scattering. The dynamic light scattering measures the equivalent hydrodynamic radius of the fibril. The Tirado formula, which relates the length of the rod-like particle to its equivalent hydrodynamic radius, was used to calculate the fibril length from the measured hydrodynamic radius. The fibril diameter was assumed to be 4 nm in the calculations. The results were shown in Fig. 3. The pure amyloid peptide solution has the highest rate of growth and they grow to an average length of 1.4 microns in 28 hours. The addition of 1, 2, and 3 mM diC_6PC can reduce the length to about 1.2, 1.0 and 0.9 microns, respectively, at 28 hours after preparation. This shows that the average length can be controlled by adding different amounts of amphiphilic molecules and at the same time the diameter of the fibrils were not significantly changed. The growth rate is much

were not significantly changed. The growth rate is much faster in the initial stage and it becomes much slower in the later stage. This could be due to the depletion of the free amyloid peptides in the later stage of fibril growth.

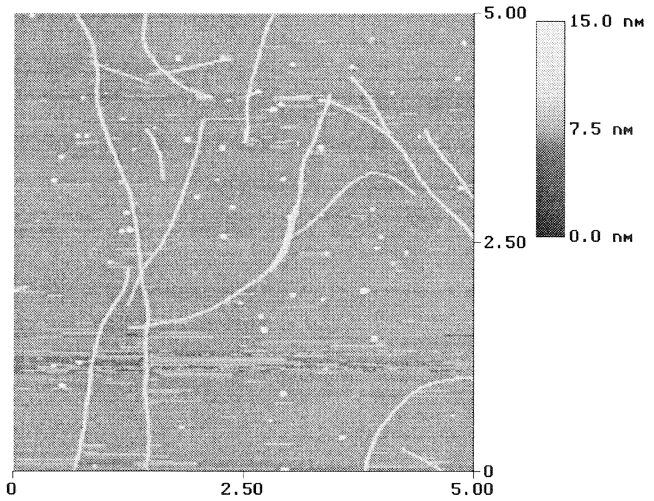

Figure 1: The AFM picture of the aggregated beta-amyloid 1-40 fibrils at 0.125 mM concentration in a 0.1 M HCl solution at 21 days.

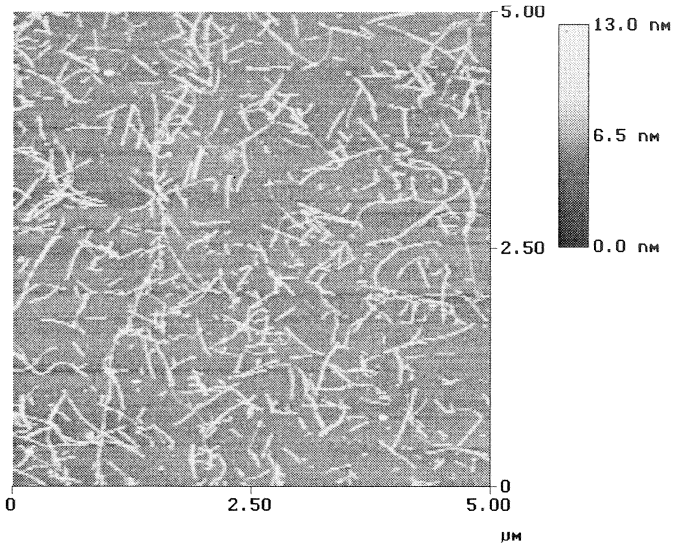

Figure 2: The AFM picture of the aggregated beta-amyloid 1-40 fibrils at 0.125 mM concentration and added with 1 mM diC_6PC in a 0.1 M HCl solution at 21 days.

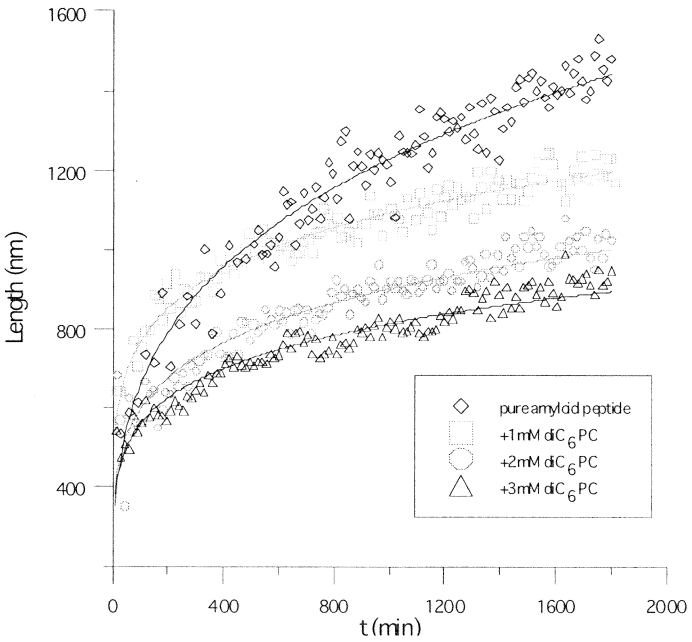

Figure 3: The average length of the aggregated beta-amyloid peptide 1-40 at 0.125 mM concentration and added with 0, 1, 2 and 3 mM diC_6PC in 0.1 M HCl solutions. The average length was measured by dynamic light scattering and calculated with the Tirado formula by assuming a fibril diameter of 4 nm.

4 SUMMARY

The growth of the fibril aggregates formed by amyloid peptide 1-40 was monitored by using dynamic light scattering and also AFM. It was found that the addition of diC_6PC could reduce the growth rate of the fibril aggregation. Eventually shorter fibrils will be formed with the addition of diC_6PC. This method can be used to control the growth process to produce fibrils with different lengths that may find applications in nanotechnologies.

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