Materials Science and Engineering C 59 (2016) 390–397

Contents lists available at ScienceDirect

Materials Science and Engineering C

journal homepage: www.elsevier.com/locate/msec

Effect of PEGylated superparamagnetic iron oxide nanoparticles (SPIONs) under magnetic field on amyloid beta fibrillation process

Somayeh Mirsadeghi [a], Saeed Shanehsazzadeh [c], Fatemeh Atyabi [a,b], Rassoul Dinarvand [a,b,*]

[a] Nanotechnology Research Center, School of Pharmacy, Tehran University of Medical Science, Tehran 1417614411, Iran
[b] Pharmaceutical Nanotechnology Department, School of Pharmacy, Tehran University of Medical Science, Tehran 1417614411, Iran
[c] Radiation Application Research School, Nuclear Science and Technology Research Institute (NSTRI), Tehran, Iran

ARTICLE INFO

Article history:
Received 10 July 2015
Received in revised form 22 September 2015
Accepted 9 October 2015
Available online xxxx

Keywords:
Superparamagnetic iron oxide nanoparticles
Magnetic field
Alzheimer's disease
Amyloid beta
Fibrillation

ABSTRACT

Superparamagnetic iron oxide nanoparticles (SPIONs) with specific surface coatings have been shown appropriate potential in the diagnosis and treatment of various brain diseases such as Alzheimer's. Comprehensive understanding of SPIONs interactions with amyloid beta (Aβ) and other amyloidogenic proteins is essential for their clinical application. SPIONs could be delivered to the target tissue under the magnetic field, while they might be influenced by the applied field. In this work, we exhibit the effect of different SPIONs (magnetized or non-magnetized with different surface charges) on the kinetics of Aβ fibrillation in aqueous solution by the aid of ThT assay. The results showed that applying of magnetic field to the SPIONs influences on the Aβ fibrillation because of its effect on the size due to surface charge. It was found that under magnetic field and high concentrations of nanoparticles (SPIONs-PEG-NH_2), the Aβ fibrillation process accelerates, while at lower concentrations the fibrillation is inhibited. Furthermore, the coating charge has a considerable role in fibrillation process and the positively charged SPIONs/magnetized, at lower particle concentrations, accelerate the fibrillation compared with the negatively charged or uncharged SPIONs. This hints that SPIONs with a positive charge have dual effects on the Aβ fibrillation process. They influence on the concentration of monomeric protein in solution and thereby the nucleation time. Also, SPIONs have an effect on binding during the protein conformation.

© 2015 Elsevier B.V. All rights reserved.

1. Introduction

Nanochemistry is a major player in the fields of science and applied science, specifically in biotechnology and information engineering [1]. Nowadays, nanochemistry is directed towards nanomedicine and nanodiagnostics. However, gaining consistent nanoparticles that can be utilized for diagnostics and medicine remains a significant challenge. Moreover, the interaction of nanoparticles with biological entities such as proteins is of great importance when it comes to Alzheimer's disease (AD) [1].

The main reason of the AD is unusual folding of the monomeric Aβ which proceeds in the structure of an oligomeric state and succeeding deposition of insoluble (fibrillar) states [2]. According to previous reports, specific charge–charge interactions of the amyloidic-polypeptide structure operate a key role in the formation of the oligomeric states [3–5]. However, these reports are disputable [6] and further studies are needed to clear up the details of the oligomerization and fibrillation processes [7]. It is well-known that the aggregation kinetics of amyloidogenic proteins and peptides follow a sigmoidal kinetics, showing three phases including: nucleation (lag phase), elongation and fibrillation. Small biological molecules such as peptides and non-peptides (e.g., inositols, phenols, and indols) have been shown to interfere with the formation of fibrils by influencing the kinetics of aggregation [8–12]. Many amyloidogenic proteins have a tendency to be engaged at the surface of different substrates; hence, nanoparticles, with their small size and large surface to volume ratio, could have a significant effect on the fibrillation process [7,12,13].

Some nanoparticles, like copolymers of N-isopropylacrylamide-N-tert-butylacrylamide, gold nanospheres/nanorods, graphene [14] and SPION-dextran coated might decrease the fibrillation rate through interactions with either the monomeric amide or oligomeric compounds, leading to a diminish of the concentration of the monomers/oligomers in resolution, and resulting in a big increase within the lag time and therefore inhibition of fibrillation [7,13,15]. It has been shown that the concentration of amine-modified phenylethylene nanoparticles influences on the fibrillation rate via acceleration of the fibrillation through the reducing of the lag phase (at low particle concentration) and inhibiting of the fibrillation at high particle concentration, suggesting a dual effects on the speed of Aβ fibrillation [16].

Among the different nanoparticles employed in biomedical research, functionalized super-paramagnetic iron oxide nanoparticles (SPIONs) have been recognized as promising materials due to their high biocompatibility, unique magnetic properties, and their capacity for use as

* Corresponding author at: Nanotechnology Research Center, School of Pharmacy, Tehran University of Medical Science, Tehran 1417614411, Iran.
E-mail address: dinarvand@tums.ac.ir (R. Dinarvand).

http://dx.doi.org/10.1016/j.msec.2015.10.026
0928-4931/© 2015 Elsevier B.V. All rights reserved.

multimodal contrast agents [17–20]. However, the application of SPIONs in the clinics in the context of diagnosis of brain diseases is still very restricted [21–24]. There is potential for the nanoparticles with high affinity for the circulating Aβ forms to persuade a "sink effect" [7,25] and thus, potentially improve AD. Therefore, SPIONs are proposed for application as theranostic agents (i.e., concurrent diagnosis and treatment) in different brain diseases [18,26,27]. Although the studies are still in their infancy, SPIONs are recognized as the most eminent candidate for multitask simultaneous biomedical applications [28–30], while the impact of magnetic field on SPIONs is of particular importance [11,31–33]. As previously mentioned, magnetic field has been used for the therapeutic applications of SPIONs [34–36] and the effect of SPIONs on amyloid beta fibrillation process has also been studied [7,26]. However the main purpose of this paper was to evaluate the impact of magnetic field on PEG coated SPIONs with different surface charges on amyloid fibrillation process.

2. Materials and methods

2.1. Super-paramagnetic iron oxide nanoparticles

Details of three SPIONs investigated are shown in Table 1, which give information on hydrodynamic particle size, composition and coating as provided by the manufacturer (Micromod Partikeltechnologie GmbH, Germany) [37]. All three SPIONs were formulated as single-domain iron crystal structure. According to the manufacturer description, PEGylated-SPIONs have 300 kDa PEG chain. The Aβ (1–2) peptide (MDAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVVIA) and Thioflavin T were used as purchased (Sigma).

2.2. Magnetic field

All samples of SPIONs for 10 min are influenced by magnetic field 1.5 Tesla at MRI Gunter. Then, the magnetized-SPIONs are characterized with TEM and DLS techniques.

2.3. Transmission electron microscopy (TEM)

A volume of 0.5 μL of dispersion (Aβ or Aβ plus SPIONs) was transferred onto carbon coated 300 mesh-Cu grids and blotted with filter paper. Fibrils were stained with 3% uranyl acetate (5 μL for 1 min), blotted, and air-dried. Transmission electron microscopy analysis was conducted with TEM BOSCH at an acceleration voltage of 80 kV.

2.4. SPION characterization

Dynamic light scattering (DLS) measurements were performed with a Malvern Zetasizer Nano ZS90 instrument equipped with a 256-channel correlator. The 488.0 nm line of a Coherent Innova-70 Ar ion laser was used as the incident beam. The used laser power was 250 mW. The scattering angles, θ, employed ranged between 40° and 140°. The temperature was maintained constant at 25 °C.

2.5. Protein fibrillation experiments

Aβ (M1-42) was dissolved in a 50:50 mixture of 0.1% NH_4OH and 100 mM Tris buffer, 0.02% NaN_3 pH 7.4 (Roughly 1 mg in 1 mL total volume). Solutions were ultracentrifuged for 1 h at 65 krpm and 4 °C in a Beckman ultracentrifuge so as to get rid pre-existing amyloid fibrils. The upper 75% of the supernatant was collected and the concentration of Aβ (M1-42) determined from its UV–Vis absorbance at 275 nm, which obtained by a Shimadzu UVmini-1240 UV–Vis Spectrophotometer (Japan).

$$C = A/\varepsilon$$

where

C concentration (molar)
A absorption (arbitrary units)
ε extinction coefficient (M^{-1} cm^{-1}) and
$\varepsilon^{275\ (A\beta)}$ 1400 M^{-1} cm^{-1}.

The supernatant was then diluted to 0.1 and 10 μM with 13 mM sodium phosphate buffer, 0.02% NaN_3, pH 7.4. 90 μL of (0.1/10 μM Aβ (M1-42) with 200 μM ThT (from a 2 mM stock solution in water)) per well was incubated in the absence or presence of 10 μL nanoparticles per well at 37 °C and shaken at 700 rpm in a 96 well black fluorescence plate, NUNC 96 black Polypropylene MicroWell™ Plates, with a shaking orbit of 3 mm. Measurements were made at regular intervals (every 5 min) using a microplate reader (Hybrid Technology™ Synergy H4 Performance (BioTek Instruments, Inc., Winooski, Vermont, USA)) with excitation and emission at 440 and 480 nm, respectively. Each experimental point is an average of the fluorescence signal of 3–12 wells containing aliquots of the same solution (same particle and protein concentration). In experiments to measure fibrillation, the NPs concentrations were fixed at 100 μg/mL. In order to stop depletion of $A\beta_{42}$ from solution as a result of adherence of $A\beta_{42}$ to the plates' chamber walls, the plates were pre-coated with poly ethylene glycol (PEG). Briefly, the PEG was diluted to 0.01 M exploitation Millipore immoderate pure water. 300 μL of this solution was aliquoted into every well of the 96-well plates and incubated at room temperature for 60 min. The wells were then aspirated completely and rinsed with 10 times their volume (3 mL) of Millipore ultra-pure water. The plates were allowed to dry at room temperature before use.

3. Results and discussion

It is surely understood that an iron atom has a strong magnetic because of its four unpaired electrons in 3d shell. Fe^{2+} has likewise four unpaired electrons in 3d shell, while Fe^{3+} possesses 5 unpaired electrons in 3d shell. Thus, the iron atoms could be formed in the crystals in para, dia or ferromagnetic states. In spite of para and diamagnetic, in ferromagnetic materials their attractive properties proceed with notwithstanding when the outer attractive field is evacuated. These materials are generally alluded to as magnets [38–40]. Inside of a magnet there are distinctive locales or domains varying each of them towards the magnetic moments' arrangement. As the size of these materials is diminished, the observed domain is limited to just a single domain. These single-domain magnets adjust all their magnetic moments in the same course, so that when an external magnetic field is connected the resulting magnetization is the biggest workable for that particular material and size. Here comes the superparamagnetic conduct, which imparts to paramagnetism the unlucky deficiency of polarization

Table 1
Nomenclature and surface coatings of SPIONs investigated.

Sample no.	Product code	Product name	Surface	Ø	Concentration	VSM[a]
1	79–55-201	Nanomag®-D-spio	PEG 300-NH2	20 nm	5 mg/mL	54 emu/g iron (H = 1000 Oe)
2	79–56-201	Nanomag®-D-spio	PEG 300-COOH	20 nm	5 mg/mL	54 emu/g iron (H = 1000 Oe)
3	79–54-201	Nanomag®-D-spio	PEG 300	20 nm	5 mg/mL	54 emu/g iron (H = 1000 Oe)

[a] Vibrating sample magnetometer.

Download English Version:

https://daneshyari.com/en/article/7868669

Download Persian Version:

https://daneshyari.com/article/7868669

Daneshyari.com