Morphology transformation between nanofibres and vesicles controlled by ultrasound and heat in tryptamine-based assembly

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ABSTRACT
A novel low-molecular-mass organic gelator T1 containing tryptamine and sugar segments was designed and synthesised which can gelate alcohols accelerated by heat and sonication. Interestingly, morphology exchange between vesicles as precipitate and a three-dimensional gel network tuned by heating and ultrasound was observed. The mechanism was studied by IR, FL, X-ray diffraction. It was presented that the effect of ultrasound was to disturb the spontaneous self-assembly of T1 molecule, and promote the long arrangement and disordered assembly of T1 molecules into fibrous networks, thus resulting in the gelation in methanol.

1. Introduction
Self-assembly in supramolecular chemistry has a great significance in understanding the origin of life and biology relevant processes (1–4). One of the main challenges is to design stimuli-responsive supramolecular building blocks endowed with functions (5–17). Hollow structures such as vesicles and tubes constructed by organic species have received considerable attention owing to their applications in the field of drug delivery, biomaterials and food processing (18, 19). The great importance is the dynamic character of vesicles since their functions could be tuned with the morphology shaping (15). Recently, functional assembly derived from natural products are found promising applications in tissue engineering, drug delivery as well as diagnostics. Tryptamine is the product of tryptophan by decarboxylic reaction, which plays a very significant role in biogenic amine-based synaptic physiology and controlling on the blood pressure. Therefore, studying the functional assembly of tryptamine derivative was favourable for understanding tryptamine-relevant biological events (20, 21).

In this decade, ultrasound waves as a kind of high-frequency mechanical stress are found to promote gel formation in material chemistry through the adjustment of non-covalent interactions via cavity effect (22, 23). Rheology and morphology switching tuned by ultrasound and heat stimuli were paid great attention in recent years. In our previous work, we used a classic of naphthalimide-based derivatives for fabricating different kinds of nano/microstructures including spheres, nanofibrils, vesicles and core-shells, which could response to ultrasound by morphology transition (24–31). However, the morphology control by ultrasound based on biomolecular assembly was rarely reported. In this work, we synthesised and evaluated a new organogelator T1 containing tryptamine moiety as showed in Scheme 1, and the reversible morphology conversion between vesicle and fibre controlled by ultrasound and heat was achieved.

2. Results and discussion
The synthesis and characterisation of T1 could be seen in supporting information. The compound T1 (25 mg/mL), when heated to a sol, and then cooled in different
Scheme 1. The chemical structure of T1.

Figure 1. (Colour online) Illustration of ultrasound-accelerated gelation of T1.

Figure 2. (Colour online) (a) UV–Vis spectra of T1 solution (10^{-4} M) and gel; (b) UV–Vis spectra of T1 suspension and gel (25 mg/mL).

Figure 3. SEM images of T1 assembly. (a) The precipitate of T1 from methanol (25 mg/mL); (b) the magnification picture of a), insert picture: TEM image of the vesicles; (c) the S-gel of T1; (d) magnification picture of c), insert picture: TEM image of ribbons of T1. Scale bar: (a) 4 μm; (b) 1 μm, insert picture: 200 nm; (c) 5 μm; (d) 1 μm, insert picture: 200 nm.
organic solvents, only precipitate or sol could be observed. Surprisingly, upon dissolving T1 powder (25 mg/mL, obtained from column) in alcohols with sonication for seconds (<20 s), fluorescent and opaque organogels formed immediately (Figure 1, Table 1).

As a typical example, the gelation behaviour of T1 in methanol was studied in detail. The aggregation information of naphthalimide segment could be deduced by UV–Vis spectra. From Figure 2, the peak at 435 nm of T1 in solution state (10⁻⁴ M) was attributed to the ICT process of 4-amino-naphthalimide group. Whilst, in the gel state, 14-nm red shift was observed compared with that of solution, indicating the J aggregate of 4-amino-naphthalimide groups in gel state. In previous work, we reported that the ICT process of naphthalimide derivative was highly dependent on the aggregation state of fluorophore (31). As seen in Figure 2(c), by in situ fluorescent examination, the intensity of S-gel quenched by 1.2 fold compared with that of the suspension (precipitate from methanol, 25 mg/mL), reflecting the ultrasound responsive properties of T1 assembly with fluorescence signal output.

Scanning electron microscopy (SEM) experiments were performed to study the microstructures of T1 aggregates controlled by heating–cooling process and ultrasound stimulus. Seen from Figure 3(a), by heating–cooling process, T1 assembled to nanovesicles with diameters range from 50 to 900 nm, and the broken vesicles could be also observed. Transmission electron microscopy (TEM) image revealed that the thickness of the vesicles was around 20 nm. However, when the S-gel was formed triggered by sonication, the SEM and TEM images of the xerogel sample showed large area of ribbons with a width range from 20 to 50 nm. Moreover, in some other areas, both vesicles and short fibrils (ribbons) coexisted in the gel system, revealing that the T1 molecules were spontaneously prone to form vesicle structure (Figure 4).

The infrared spectra of T1 precipitate and S-gel confirmed the hydrogen bonding interaction between amide groups. Seen from Figure 5, The –NH and C=O bands moved from

| Solvent   | H–C | S     |
|-----------|-----|-------|
| Water     | S   | P     |
| n-propanol| P   | OG    |
| methanol  | P   | OG    |
| ethanol   | P   | OG    |
| butanol   | P   | OG    |
| ethyl acetate | I | I     |
| acetone   | I   | I     |
| chloroform| I   | I     |
| DMSO      | S   | S     |
| DMF       | S   | S     |
| acetonitrile | I | I     |

Note: P: precipitate; i: insoluble; S: sol; OG: opaque gel.

Figure 4. (a) SEM images of T1 S-gel in other area; (b) the magnification picture of a). Scale bar: (a) 5 μm; (b) 2 μm.

Table 1. The gelation properties of T1 (25 mg/mL) in organic solvents.

Figure 5. (Colour online) (a) FT-IR spectra of T1 precipitate and S-xerogel; (b) XRD data of T1 precipitate and S-xerogel.
3379 and 1639 cm\(^{-1}\) in the precipitate to 3373 and 1645 cm\(^{-1}\), respectively, which indicated the formation of much stronger hydrogen bonding of T1 assembly after sonication. To gain a deep insight into the assembly mechanism, powder X-ray diffraction (XRD) experiment was carried out. The XRD signals of T1 precipitate showed peaks at 1.8, 1.2 and 0.9 nm, which was with the ratio of 1.2/3:1/2, indicating the lamellar packing of molecules. The distance of 1.8 nm was closed to the bent structure of single T1 molecule. The peaks at 1.6 and 1.4 nm of the S-xerogel in methanol revealed a more bent molecule and different aggregation mode than that found in T1 precipitate.

From the above results, our findings could be summarised as following: by the classic heating–cooling process, T1 molecules assembled regularly to nanovesicles as lamellar structure through non-covalent interactions such as hydrogen bonding, π stacking, as well as hydrophilic interactions. When the dissolved through non-covalent interactions such as hydrogen bonding, π molecular interactions. The effect of ultrasound was to disturb the molecular interactions. The effect of ultrasound was to disturb the molecular interactions. The effect of ultrasound was to disturb the molecular interactions. The effect of ultrasound was to disturb the molecular interactions. The effect of ultrasound was to disturb the molecular interactions. The effect of ultrasound was to disturb the molecular interactions. The effect of ultrasound was to disturb the molecular interactions. The effect of ultrasound was to disturb the molecular interactions. 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