pH responsive and size-controllable vesicles from terminal-carboxyl hyperbranched polyester

Tianliang Li, Jilu Chen, Zhijun Hang & Sheng han*

Shanghai institute of technology, Fengxian, Shanghai, China

Abstract. Amphiphilic carboxyl-terminated Hyperbranched Polyester (c-HBPE) is synthesized by 1,2,4-Benzenetricarboxylic anhydride（BTAA）and 1,6-hexanediol. The structure of c-HBPE is characterized by FT-IR, 1H-NMR, GPC. Vesicles of c-HBPE are fabricated by aqueous self-assembly. Results of Transmittance Measurement(TM), DLS, Zeta potential indicated pH responsive of c-HBPE vesicles . Size of vesicles can be controlled from 2μm～200nm by adjusting the solution pH. Such materials can be used as drug encapsulation and release.

Introduction

Polymer vesicles, commonly called polymersomes, are spherical shell structures in which an aqueous compartment is enclosed by a bilayer membrane made from amphiphilic block copolymers[1]. Because of the high molecular weight of these block copolymers, polymer vesicles have superior stability and greater toughness than liposomes[2]. More interestingly, their membrane properties can be extensively tailored using polymer chemistry[2-4]. This unique design flexibility opens new opportunities for their use in applications such as encapsulation and targeted drug delivery, as nanoreactors and as templates for micro- and nano-structured materials.

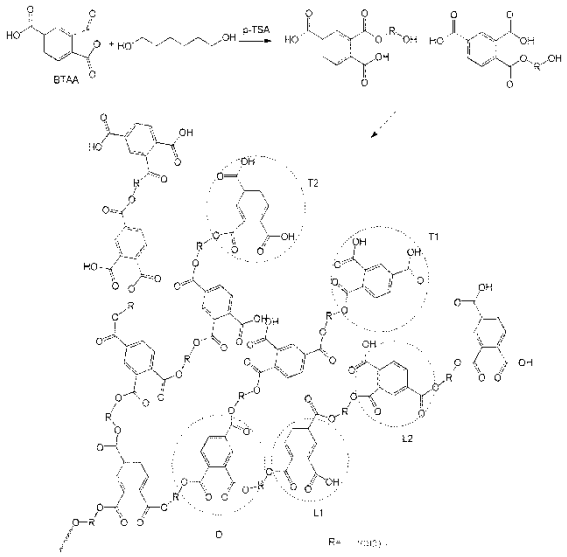
Stimuli-responsive disassembly and reassembly of supramolecular assemblies play a significant role in realizing their biological functions[5]. Inspired by this, considerable effort has been devoted to the design and development of structurally well-defined assemblies with fascinating properties and intriguing functions for their diverse applications in chemistry, biology, and materials science[6]. The pH is an important signal, which can be addressed through pH-responsive materials. Ionisable polymers with a pKa value between 3 and 10 are candidates for pH-responsive systems . Weak acids and bases like carboxylic acids, phosporic acid and amines, respectively, exhibit a change in the ionisation state upon variation of the pH.

Herein, we report a pH responsive and size-controllable vesicle from terminal-carboxyl hyperbranched polyester. Such materials can be used as drug encapsulation and release.

Experimental section

Synthesis, characterization and self-assembly of amphiphilic hyperbranched polyesters

c-HBPE is synthesis by one-pot reaction. Three-neck flask is loaded with BTAA (19.2g, 0.1mol), 1,6-hexanediol (11.8g, approximately 0.1mol), p-TSA (1g, 0.0058mol) and tetrahydrofuran (50mL). The mixture is stirred at room temperature for 12 hours. Then the mediate is agitated by mechanical agitator at 80 ^{o}C for 1 hour, 100 ^{o}C for 1 hour and 120 ^{o}C for 4 hours. All the progress of reaction is under nitrogen atmosphere. The crude is dissolved in 30ml DMF and precipitated in 1000ml methanol. The product is dried overnight in a vacuum oven at 35 ^{o}C. Finally, the yield of c-HBPE is 75%. The detail process of synthesis of c-HBPE is shown as scheme 1.



Scheme 1. Synthesis of c-HBPE

Structrue of c-HBPE is characterized by FT-IR,^{1}H-NMR,GPC. Figure 1 is FT-IR spectrum of c-HBPE. As Figure 1 shows we can see the stretch vibration absorption spectra of -CH_2-,C=O and C-O-C at 1920 cm^{-1},1725 cm^{-1} and 1250 cm^{-1}. It indicated that a large number of ester group generated between anhydride groups and hydroxy groups is existing in c-HBPE. Obviously, stretch vibration absorption spectra of -OH at 3400 cm^{-1} is almost disappeared from intermediate which indicated that polymerization reaction occurred.

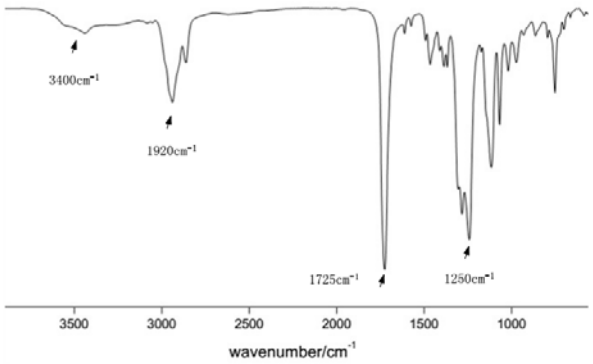


Figure 1. FT-IR spectrum of c-HBPE

Figure 2. is ^{1}H-NMR of c-HBPE. As Figure 2 shows that 7.5-8.5(3H, phenyl),4.2(2H,-CO-O-CH_2-),1.5-1.8(2H,-O-CH_2-CH_2-),1.2-1.5(2H,-O-CH_2-CH_2-CH_2-),2.48(DMSO). Amplification and integration of chemistry shift among 7.5-8.5 and put D, L, and T into (D+T)/(D+L+T), DB(Degree of Branching) is 48.7%. D, L and T is marked in scheme 1.

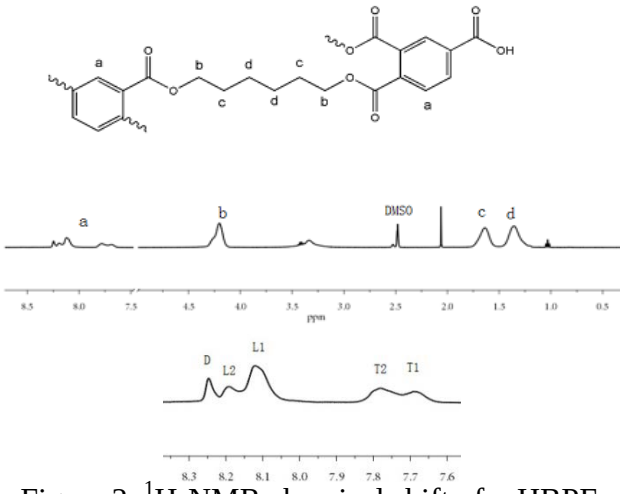


Figure 2. ^{1}H-NMR chemical shift of c-HBPE

Molecular weight of c-HBPE is measured by GPC. As Figure 3 shows that Mn of c-HBPE is 3.4 kDa and Mw/Mn is 1.894.

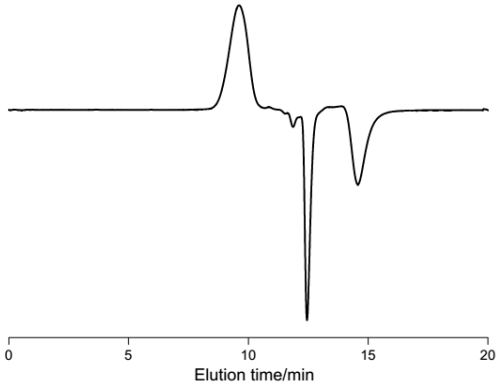


Figure 3.GPC data of c-HBPE

c-HBPE vesicles are fabricated by synchronous-assembly approach. 0.01g c-HBPE is dissolved in little acetone and drop 50ml deionized water into the solution by fast stirring. Stop stirring until the opalescence is obvious. The topology of vesicles is observed by OM (Optical Microscope), SEM and TEM (Figure4) . As Figure 4 shows we can find the hollow structure of vesicles.

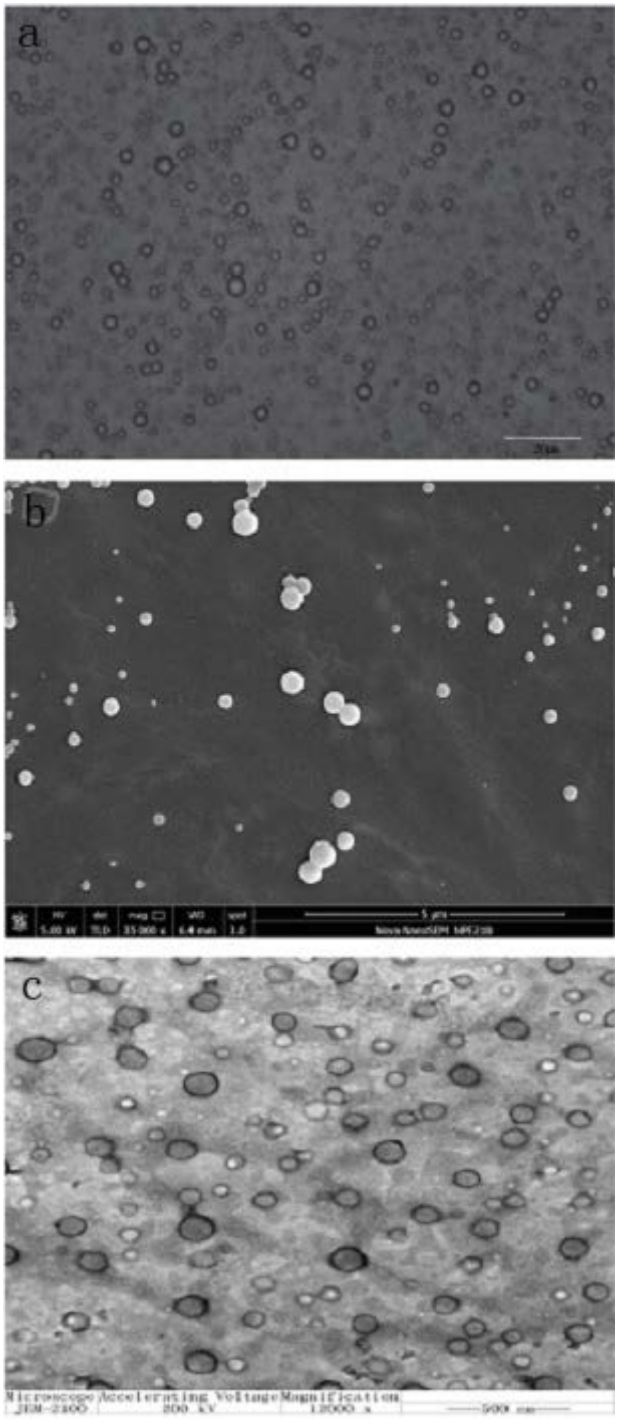


Figure 4. OM(a), SEM(b) and TEM(c) of c-HBPE vesicles. Vesicles(TEM) is stained by phosphotungstic acid.

pH responsive of c-HBPE vesicles

To our great surprise, c-HBPE demonstrated an interesting pH-responsive self-assembly behavior in water. First, the pH-sensitivity is highlighted by a visible change of the light transmittance of c-HBPE aqueous solutions with different pH values as shown in Figure 5a and Figure 5b. Evidently, there is a clear turbidity jump with decreasing pH for c-HBPE solution. The solution at near-neutral pH is transparent. However, it becomes totally cloudy at pH 3.5. Such a turbidity jump is certainly associated with a morphology transition of the supramolecular aggregates.

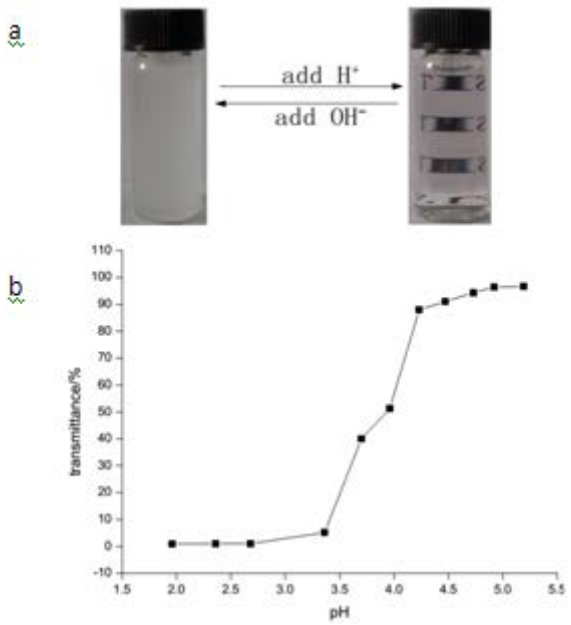


Figure 5. Transmittance versus the pH value curve

DLS is used to further characterize size of c-HBPE vesicles. Figure 5b shows the relationship between pH and vesicle sizes. As shown in Figure 6, c-HBPE vesicles have a similar size above pH=5.0, But when the solution pH is loared, an obvious point occurs in the vesicle size versus the pH value curve. However, the vesicles in a more acidic aqueous solution (pH<2.5) are not stable and would settle from the solution under the force of gravity.

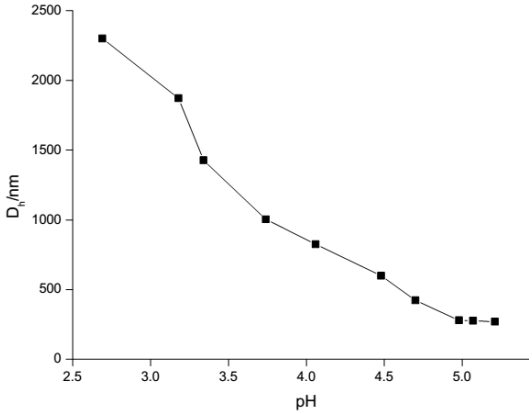


Figure 6.size of c-HBPE versus the pH value curve

Zeta potential measurements is used to characterize the surface potential of c-HBPE vesicles. As Figure 7a shows that value of Zeta potential below pH=2.5 or above pH=5.0 tends to be stable which indicates that the pH responsive is relevant to terminal carboxyl and there is a ionized equilibrium of c-HBPE in water(Figure 7b).

According to the results of transmittance, optical microscopy, TEM, SEM, DLS and zeta optional, c-HBPE will undergo a pH-responsive self-assembly process. Size of c-HBPE vesicles can be controlled from 2μm to 200nm. Such materials can be used as to construct smart release system.

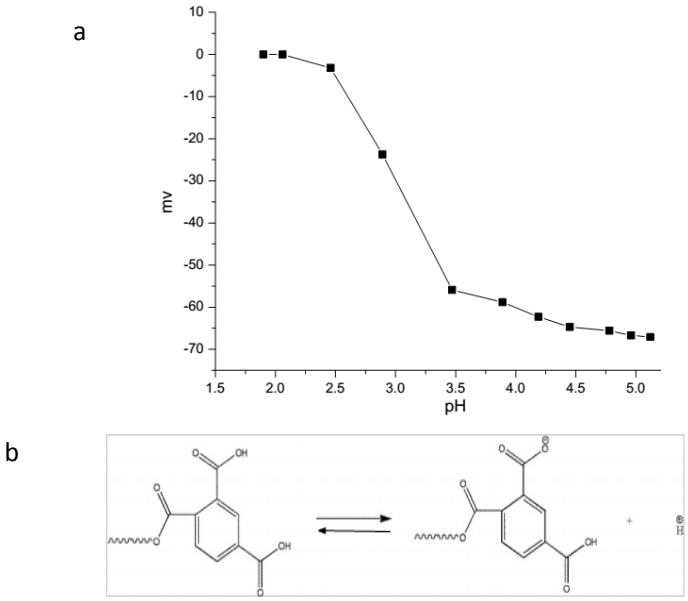


Figure 7. Zeta potential of c-HBPE(a) and ionized equilibrium of c-HBPE(b)

Conclusion

The work here reports a facile preparation of novel polymer vesicles with pH sensitivity and generation dependence by aqueous self-assembly of carboxyl-terminated hyperbranched polyester. The polymer vesicles possess several advantages: 1) a cheap and simple synthesis, 2) a convenient self-assembly process, 3) a controllable size from 200 nm to 2μm. Such advantages make the polymer vesicles attractive in subsequent applications such as drug encapsulation, release, template self-assembly.

REFERENCES

(1) Li, M. H.; Keller, P. Stimuli-responsive polymer vesicles. *Soft Matter* 2009, *5*, 927-937.

(2) Discher, B. M. Polymersomes: tough vesicles made from diblock copolymers. *Science* 1999, *284*, 1143.

(3) Zhang, L.; Yu, K.; Eisenberg, A. Ion-Induced Morphological Changes in "Crew-Cut" Aggregates of Amphiphilic Block Copolymers. *Science* 1996, *272*, 1777-1779.

(4) Jjlm, C. Helical superstructures from charged poly(styrene)-poly(isocyanodipeptide) block copolymers. *Science* 1998, *280*, 1427.

(5) Liu, G.; Zhou, L.; Guan, Y.; Su, Y.; Dong, C. Multi-responsive polypeptidosome: characterization, morphology transformation, and triggered drug delivery. *Macromolecular Rapid Communications* 2014, *35*, 1673–1678.

(6) Schmaljohann, D. Thermo- and pH-responsive polymers in drug delivery. *Adv Drug Deliv Rev* 2006, *58*, 1655–1670.