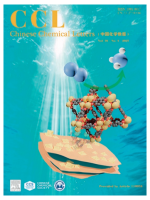
Chinese Chemical Letters 36 (2025) 109820

Contents lists available at ScienceDirect

Chinese Chemical Letters

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



One-step preparation of biocompatible amphiphilic dimer nanoparticles with tunable particle morphology and surface property for interface stabilization and drug delivery

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ARTICLE INFO

Article history:
Received 18 January 2024
Revised 21 March 2024
Accepted 22 March 2024
Available online 22 March 2024

Keywords:
Janus particle
Amphiphilic particle
Dimer particle
Colloidal surfactant
Pickering emulsion
Drug delivery

ABSTRACT

Biocompatible amphiphilic nanoparticles (NPs) with tunable particle morphology and surface property are important for their applications as functional materials. However, previously developed methods to prepare amphiphilic NPs generally involve several steps, especially an additional step for surface modification, greatly hindering their largescale production and widespread applications. Here, a versatile one-step strategy is developed to prepare biocompatible amphiphilic dimer NPs with tunable particle morphology and surface property. The amphiphilic dimer NPs, which consist of a hydrophobic shellac bulb and a hydrophilic poly(lactic acid) (PLA) bulb with PLA-poly(ethylene glycol) (PEG) on the bulb surface, are prepared in a single step by controlled co-precipitation and self-assembly. Amphiphilic PLA-PEG/shellac dimer NPs demonstrate excellent tunability in particle morphology, thus showing good performances in controlling the interfacial curvature and emulsion type. In addition, temperature-responsive PLA-poly(*N*-isopropyl acrylamide) (PNIPAM)/shellac dimer NPs are prepared following the same method and emulsions stabilized by them show temperature-triggered response. The applications of PLA-PEG-folic acid (FA)/shellac dimer NPs for drug delivery have also been demonstrated, which show a very good performance. The strategy of preparing the dimer NPs is green, scalable, facile and versatile, which provides a good platform for the design of dimer NPs with tunable particle morphology and surface property for diverse applications.

With the advances of science and technology, isotropic nanoparticles (NPs) with symmetric structure and property could no longer meet the growing demand [1,2]. Anisotropic NPs with asymmetric structure and property are attracting more and more attention [3,4]. Among the anisotropic NPs, Janus NPs with two distinct bulbs or surfaces have demonstrated widespread applications in color display [5,6], interfacial catalyst [7,8], emulsion stabilization [9–11], bio sensing [12–14], and drug delivery [15,16]. For example, the applications of amphiphilic Janus NPs with one bulb hydrophilic and the other hydrophobic have been extensively explored as colloidal surfactants [17,18], which could overcome the coalescence and Oswald ripening of molecular surfactant-stabilized emulsions, thus achieving long-term stability [19,20]. In addition, Janus NPs could also perform as drug delivery vehicles, which have been proven to improve drug stability and bioavailability, prolong cycle time, increase accumulation and uptake at tumor sites, reduce drug toxicity and side effects, and overcome the shortcomings of traditional therapies [21–23].

To prepare amphiphilic Janus NPs, various methods have been developed, such as selective surface modification [24], microfluidics-based template [25,26], molecular self-assembly [27], polymerization-induced phase separation [28], and nucleus-aided growth [29]. Despite of all the advances, each method has its

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https://doi.org/10.1016/j.cclet.2024.109820

advantages and disadvantages. For example, selective surface modification is limited by its low yield [30]; amphiphilic Janus NPs prepared using microfluidics-based templates are micron size [31]; molecular self-assembly is limited to some specific molecules [32]; polymerization-induced phase separation generally lacks biocompatibility [33]; nucleus-aided growth [34] is difficult to load actives. Therefore, a facile green method to prepare biocompatible amphiphilic Janus NPs is essential.

Co-precipitation upon rapid solvent exchange is a facile and green method to prepare biocompatible NPs [35–37]. However, NPs with an isotropic spherical shape are generally achieved upon co-precipitation [38]. Recently, dimer NPs consisted of two distinct bulbs are prepared by controlled co-precipitation and phase separation [9]. However, the selective surface modification of the dimer NPs to achieve amphiphilicity generally requires an additional chemical or physical treatment step, which greatly complicates the preparation process. Therefore, it is still a great challenge to develop a facile green method to prepare biocompatible amphiphilic Janus NPs with tunable particle morphology and surface property.

Here, a versatile strategy is developed to prepare biocompatible amphiphilic dimer NPs with tunable particle morphology and surface property in a single step based on controlled co-precipitation and self-assembly. Upon rapid solvent exchange, shellac, poly(lactic acid) (PLA) and PLA-poly(ethylene glycol) (PEG) co-precipitate and self-assemble to form amphiphilic PLA-PEG/shellac dimer NPs. The NP size could be tuned by the polymer concentration, while the NP shape could be tailored by the polymer concentration ratio. The amphiphilic dimer NPs are excellent colloidal surfactants with the hydrophobic shellac bulb preferring the oil phase and the hydrophilic PLA-PEG bulb preferring the water phase, mimicking nonionic molecular surfactants. The flexible tuning of NP shape provides a good control of the interfacial curvature and emulsion type that amphiphilic dimer NPs with the hydrophilic PLA-PEG bulb larger than the hydrophobic shellac bulb could better fit the interface of oil-in-water emulsions. The dependances of emulsion size on homogenization strength and NP concentration are also investigated in detail. To demonstrate the versatility of the NP preparation method, temperature-responsive PLA-poly(*N*-isopropyl acrylamide) (PNIPAM)/shellac dimer NPs are prepared and emulsions stabilized by them show temperature-triggered response. In addition, the flexible tuning of NP shape and property makes it easy to enhance the cellular uptake to improve the drug delivery efficiency of PLA-PEG-folic acid (FA) dimer NPs. The preparation strategy is facile and the dimer NPs are tunable, which greatly facilitates their largescale production and widespread applications.

To prepare amphiphilic PLA-PEG/shellac dimer NPs in a single step, shellac, PLA and PLA-PEG, whose chemical structures are shown in Fig. S1 (Supporting information), are co-dissolved in tetrahydrofuran, and the solution is quickly injected into a water reservoir through a tapered nozzle, as schematically shown in Fig. 1a. Upon rapid solvent exchange, shellac, PLA and PLA-PEG co-precipitate and phase-separate to form amphiphilic dimer NPs with PLA-PEG preferentially decorating the PLA bulb surface, as modeled in Fig. 1b. The NP formation involves both the nanoscale self-assembly of PLA-shellac dimer NPs and the subsequent molecular self-assembly of PLA-PEG on the PLA bulb surface. During the self-assembly process, PLA-PEG, the amphiphilic bock-copolymer, plays two important roles. First PLA-PEG has a hydrophobic block of PLA and a hydrophilic block of PEG, which prefers to deposit at the PLA/water interface and performs as a molecular surfactant to tune the interfacial tension and thus the NP shape, as shown in Fig. S2 (Supporting information). The presence of PLA-PEG will decrease the PLA/water interfacial tension, favoring $\gamma_{S/P} < \gamma_{S/W} \sim \gamma_{P/W}$ and thus a dimer structure. Otherwise, PLA and shellac will form a more spherical shape. Second, PLA-PEG preferentially decorates the PLA bulb surface and thus functionalizes the dimer NPs. Both of shellac and PLA are relatively hydrophobic, showing water contact angles of 76° and 73°, respectively, as shown in Figs. S3a and b (Supporting information). In contrast, PLA-PEG only has a small water contact angle of 15° (Fig. S3c in Supporting information) and the functionalization of PLA-PEG makes the PLA-PEG/shellac dimer NPs amphiphilic.

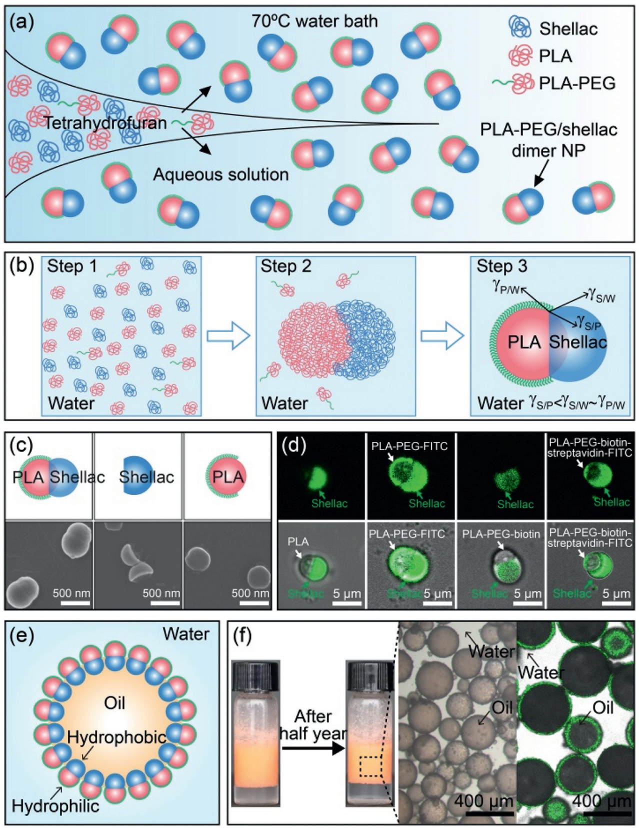

Fig. 1. One-step preparation of biocompatible amphiphilic dimer NPs with tunable particle morphology and surface property. (a) Schematic illustration showing the formation of amphiphilic PLA-PEG/shellac dimer NPs upon rapid solvent exchange and controlled co-precipitation. (b) Self-assembly of PLA-PEG/shellac dimer NPs. (c) SEM images of PLA-PEG/shellac dimer NPs (left), crescent moon-like shellac bulbs (middle) and aspherical PLA bulbs (right). (d) Fluorescent and overlay images of PLA-PEG/shellac, PLA-PEG-FITC/shellac, PLA-PEG-biotin/shellac and PLA-PEG-biotin-streptavidin-FITC/shellac dimer NPs. (e) Model of an NP-stabilized oil droplet. (f) Photographs and optical microscope images of oil-in-water emulsions stabilized by amphiphilic PLA-PEG/shellac dimer NPs. If not specified, dimer NPs are prepared using 10 mg/mL shellac and 10 mg/mL PLA with 2.5% PLA-PEG. The volume ratio of water to oil is 1 to 1.

The dimer structure of PLA-PEG/shellac NPs is confirmed by selectively dissolving the shellac bulb or the PLA-PEG bulb, as shown in Fig. 1c. For example, by selectively dissolving the PLA-PEG bulb using ethyl acetate, only the crescent moon-like shellac bulb is left. In contrast, by selectively dissolving the shellac bulb using alkaline solution, the aspherical PLA-PEG bulb is observed. *In situ* EDX spectra also suggest that the local chemical contents of the PLA-PEG bulb are different from those of the shellac bulb, as shown in Figs. S4a and b (Supporting information). In addition, the local chemical contents of the PLA-PEG bulb are richer in oxygen than those of the PLA bulb, suggesting the enrichment of PLA-PEG on the PLA bulb surface. To further confirm that PLA-PEG selectively decorates the PLA bulb surface, PLA-PEG-FITC/shellac and PLA-PEG-biotin/shellac dimer NPs are prepared following the same procedure as PLA-PEG/shellac dimer NPs, as shown in Fig. 1d. In PLA-PEG/shellac dimer NPs, the shellac bulb has weak fluorescence while the PLA-PEG bulb shows no fluorescence. When a fluores-

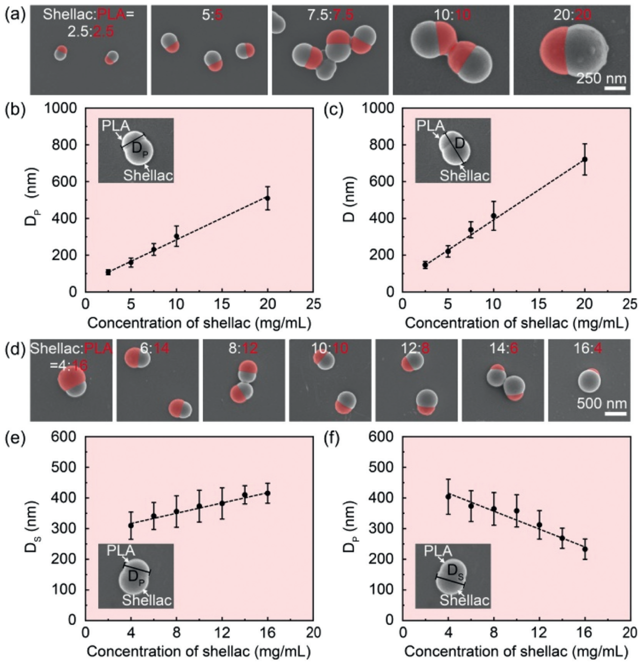

Fig. 2. Amphiphilic PLA-PEG/shellac dimer NPs with tunable size and shape. (a) SEM images of dimer NPs prepared with a same concentration of shellac and PLA ($C_{\text{shellac}} = C_{\text{PLA}}$), while the concentrations of shellac and PLA increase from 2.5 mg/mL to 20 mg/mL. (b) PLA bulb diameter (D_{P}) and (c) dimer NP diameter (D) as a function of shellac concentration. Shellac and PLA have a same concentration. (d) SEM images of dimer NPs prepared with a same total concentration of $C_{\text{shellac}} + C_{\text{PLA}} = 20$ mg/mL, while the concentration ratio of C_{shellac}:C_{PLA} increases from 4:16 to 16:4. (e) Shellac bulb diameter, D_{S}, and (f) PLA bulb diameter, D_{P}, as a function of shellac concentration. The total concentration of $C_{\text{shellac}} + C_{\text{PLA}}$ is kept constant at 20 mg/mL. Data are presented as mean ± standard deviation (SD) (n = 60).

cence group (FITC) is functionalized at the end of PLA-PEG, the PLA-PEG-FITC bulb shows a clear fluorescence signal around the bulb surface. In addition, the PLA-PEG-biotin bulb alone has no fluorescence. When streptavidin-FITC selectively binds to PLA-PEG-biotin through noncovalent biotin-streptavidin interaction, a clear fluorescence signal is observed around the PLA bulb surface. These results suggest that PLA-PEG has successfully and selectively decorated the PLA bulb and different functionality could be implemented on the PLA bulb through the end of PLA-PEG.

Amphiphilic PLA-PEG/shellac dimer NPs possess both a hydrophilic PLA-PEG bulb, which prefers the water phase, and a hydrophobic shellac bulb, which tends to submerge in the oil phase. Therefore, the amphiphilic dimer NPs are excellent colloidal surfactants to stabilize both oil-in-water and water-in-oil emulsions, as modeled in Fig. 1e. In contrast to molecule-stabilized emulsions, which are susceptible to coalescence and Oswald ripening, NP-stabilized emulsions possess a long-term stability, due to the strong anchoring strength of amphiphilic dimer NPs at the oil/water interface, as shown in Fig. 1f. The amphiphilic dimer NPs tend to adsorb at the oil/water interface and could stabilize both water-in-oil and oil-in-water emulsions, as shown in Fig. S5 (Supporting information), where the amphiphilic dimer NPs uniformly distributed at the interface are directly visualized by fluorescence confocal microscope due to the weak fluorescence of the shellac bulb.

The preparation method of amphiphilic PLA-PEG/shellac dimer NPs is facile and versatile. The NP size and shape could be tailored by simply tuning the polymer concentration and concentration ratio, respectively, as shown in Figs. 2a and d. When the concentration ratio of C_{shellac}:C_{PLA} is 1:1, the shellac bulb is slightly larger than the PLA bulb. This is because the crescent moon-like shellac bulb appears as a cap on the aspherical PLA bulb in each dimer NP. As the concentrations of shellac and PLA increase from 2.5 mg/mL to 20 mg/mL, the PLA bulb diameter, D_{P}, increases from 108 nm to 509 nm, while the dimer NP diameter, D, increases from 147 nm to 721 nm, as summarized in Figs. 2b and c. When the total concentration of $C_{\text{shellac}} + C_{\text{PLA}}$ is kept constant at 20 mg/mL, the shellac bulb diameter (D_{S}) increases from 310 nm to 415 nm, while the PLA bulb diameter (D_{P}) decreases from 404 nm to 233 nm, as the concentration ratio of C_{shellac}:C_{PLA} increases from 4:16 to 16:4, as summarized in Figs. 2e and f.

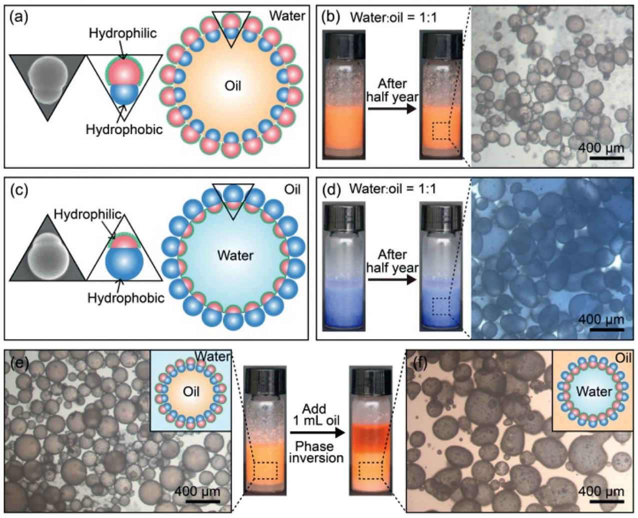

Fig. 3. Amphiphilic PLA-PEG/shellac dimer NPs with tunable shape for controlled interfacial curvature and emulsion type. (a) Schematics and (b) photographs of NP-stabilized oil-in-water emulsions when the hydrophilic PLA-PEG bulb is larger than the hydrophobic shellac bulb. The amphiphilic dimer NPs are prepared using 4 mg/mL shellac and 16 mg/mL PLA with 2.5% PLA-PEG. The volume ratio of water to oil is 1 to 1. (c) Schematics and (d) photographs of NP-stabilized water-in-oil emulsions when the hydrophobic shellac bulb is larger than the hydrophilic PLA-PEG bulb. The amphiphilic dimer NPs are prepared using 14 mg/mL shellac and 6 mg/mL PLA with 2.5% PLA-PEG. The volume ratio of water to oil is 1 to 1. Phase inversion of (e) NP-stabilized oil-in-water emulsions into (f) water-in-oil emulsions when V_{water}: V_{oil} changes from 1:1 to 1:2. The amphiphilic dimer NPs are prepared using 10 mg/mL shellac and 10 mg/mL PLA with 2.5% PLA-PEG.

Inspired by nonionic molecular surfactants, which prefer oil-in-water/water-in-oil emulsions when their hydrophilic block is larger/smaller than their hydrophobic block, amphiphilic PLA-PEG/shellac dimer NPs with tunable shape are also able to control the interfacial curvature and thus the emulsion type. For example, when the hydrophilic PLA-PEG bulb is larger than the hydrophobic shellac bulb, amphiphilic dimer NPs could better fit the oil-in-water interfacial curvature, thus favoring oil-in-water emulsions, as modeled in Fig. 3a. In contrast, when the hydrophobic shellac bulb is larger than the hydrophilic PLA-PEG bulb, water-in-oil emulsions are better stabilized, as modeled in Fig. 3c. This is directly proved by the experimental results that when amphiphilic dimer NPs prepared using 4 mg/mL shellac and 16 mg/mL PLA with 2.5% PLA-PEG, oil-in-water emulsions are stabilized, as shown in Fig. 3b. In contrast, when amphiphilic dimer NPs prepared using 14 mg/mL shellac and 6 mg/mL PLA with 2.5% PLA-PEG, water-in-oil emulsions are obtained, as shown in Fig. 3d. When the amphiphilic dimer NPs are prepared using 10 mg/mL shellac and 10 mg/mL PLA with 2.5% PLA-PEG, the hydrophobic shellac bulb has a comparable size as the hydrophilic PLA-PEG bulb, and oil-in-water emulsions are achieved, since the colloidal surfactants are previously dispersed in the water phase, as shown in Fig. 3e. Phase inversion of the NP-stabilized oil-in-water emulsions into water-in-oil emulsions occurs when V_{water}:V_{oil} changes from 1:1 to

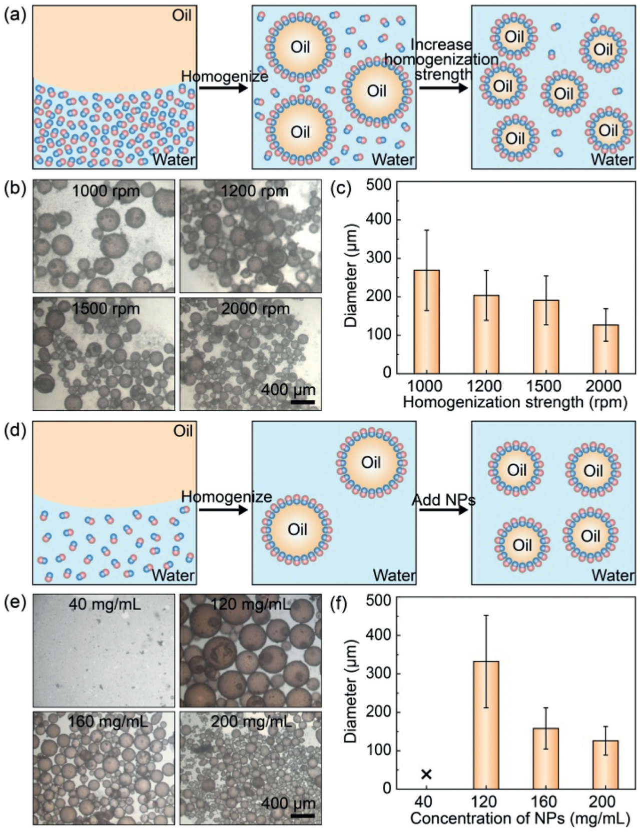

Fig. 4. Dependances of emulsion size on homogenization strength and particle concentration. (a) Schematics showing the emulsification of oil-in-water emulsions in the presence of excess colloidal surfactants. The emulsion size decreases as the homogenization strength increases. (b) Optical microscope images and (c) diameters of NP-stabilized oil-in-water emulsions prepared by different homogenization strengths. The concentration of amphiphilic dimer NPs is kept constant at 160 mg/mL. (d) Schematics showing the emulsification of oil-in-water emulsions in the presence of insufficient colloidal surfactants. The emulsion size decreases as the NP concentration increases. (e) Optical microscope images and (f) diameters of NP-stabilized oil-in-water emulsions prepared with different NP concentrations. The homogenization strength is kept constant at 2000 rpm. Data are presented as mean ± standard deviation (SD) (n = 60).

1:2, which is attributed to the catastrophic effect that the volume of the oil phase is dominant, as shown in Fig. 3f.

The dependences of emulsion size on homogenization strength and particle concentration are investigated in detail. In the presence of excess colloidal surfactants, oil-in-water emulsions are simply sheared into smaller ones as the homogenization strength increases, as modeled in Fig. 4a. This model is consistent with the experimental results of the optical microscope images in Fig. 4b and the measured diameters of NP-stabilized emulsions prepared by different homogenization strengths in Fig. 4c. Similar results are also observed when the emulsions are prepared by different stirring strengths, as shown in Fig. S6 (Supporting information). When the colloidal surfactants are insufficient and the homogenization strength is strong (*e.g.*, 2000 rpm), the emulsion size decreases as the concentration of amphiphilic dimer NPs increases, as modeled in Fig. 4d. This is because the total interfacial area that could be covered and stabilized by colloidal surfactants is determined by the NP concentration. Even though emulsions could be sheared into smaller ones by strong homogenization strength, they are not fully covered by colloidal surfactants and will coalesce into large ones until their surfaces are fully covered. Therefore, the size of NP-stabilized emulsions is limited by the NP concentration and they could be sheared into smaller ones when the NP concentration increases, as shown in Figs. 4e and f.

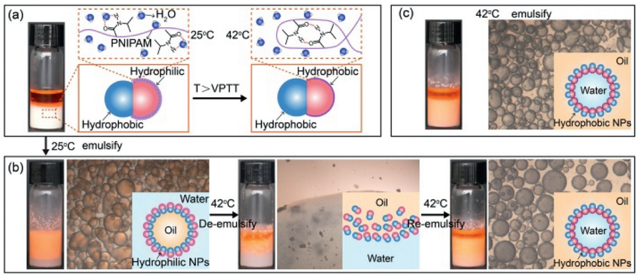

Fig. 5. Emulsification and de-emulsification of emulsions stabilized by temperature-responsive PLA-PNIPAM/shellac dimer NPs. (a) Schematics showing the reversible change between amphiphilic and hydrophobic PLA-PNIPAM/shellac NPs upon heating and cooling. (b) Photographs and optical microscope images of NP-stabilized oil-in-water emulsions emulsified at 25 °C (left), de-emulsified at 42 °C by gentle shaking (middle) and re-emulsified into water-in-oil emulsifications at 42 °C by vortexing (right). (c) Photographs and optical microscope images of NP-stabilized water-in-oil emulsions directly emulsified at 42 °C.

Amphiphilic PLA-PEG/shellac dimer NPs are excellent colloidal surfactants. They could stabilize various oil droplets in water for a long period of time. For example, silicone oil-in-water emulsions, hexadecane-in-water emulsions and perfluorohexane-in-water emulsions could all be stabilized by the amphiphilic dimer NPs. After half year, the emulsions are still stable, as shown in Fig. S7 (Supporting information).

The strategy of preparing amphiphilic dimer NPs is versatile. For example, PLA-PNIPAM, which is synthesized following the synthetic route in Fig. S8 (Supporting information) and characterized by the NMR results in Fig. S9 (Supporting information), is used to replace PLA-PEG to implement the amphiphilic dimer NPs with temperature-triggered response. PLA-PNIPAM/shellac NPs are thus prepared following the same procedure as PLA-PEG/shellac NPs, and the successful decoration of PLA-PNIPAM on the PLA bulb is confirmed by the EDX result, as shown in Fig. S4c (Supporting information). Generally, PNIPAM could reversibly change between hydrophilic and hydrophobic states upon heating and cooling, as modeled in Fig. 5a. At room temperature, PNIPAM is hydrophilic, as suggested by the small water contact angle of 11° (Fig. S3d in Supporting information), and PLA-PNIPAM/shellac NPs are amphiphilic, which is proved by the successful emulsification of oil-in-water emulsions in the presence of the NPs (left image in Fig. 5b). However, when the temperature increases to 42 °C, which is above the lower critical solution temperature of PNIPAM, PNIPAM becomes hydrophobic, as suggested by the increased water contact angle of 52° (Fig. S3e in Supporting information), and PLA-PNIPAM/shellac NPs become relatively hydrophobic, leading to the temperature-triggered destabilization of oil-in-water emulsions by gentle shaking (middle image in Fig. 5b). Since PLA-PNIPAM/shellac NPs are relatively hydrophobic at 42 °C and prefer to wet the oil phase, the de-emulsified system could be re-emulsified into water-in-oil emulsions at 42 °C by vortexing (right image in Fig. 5b). Alternatively, the system could directly be emulsified into water-in-oil emulsions when initially emulsified at 42 °C (Fig. 5c). Therefore, the type of emulsions stabilized by PLA-PNIPAM/shellac dimer NPs strongly depends on the temperature.

PLA-PEG/shellac dimer NPs are biocompatible, since both PLA and shellac are FDA-approved, and their dispersions in water are stable over time, as shown in Fig. S10 (Supporting information). To further demonstrate the biocompatibility of PLA-PEG/shellac dimer NPs, KPC and HPDE cells are co-cultured with PLA-PEG/shellac dimer NPs of different concentrations, as shown in Fig. 6a. After 24 h' co-culture, no significant differences are observed in their cell viability even when the concentration of PLA-PEG/shellac dimer

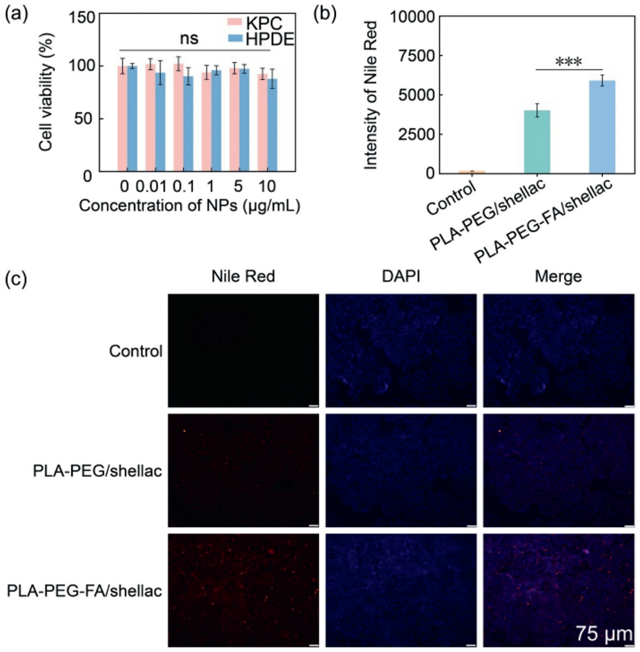

Fig. 6. Biocompatibility and drug delivery performances of PLA-PEG/shellac and PLA-PEG-FA/shellac dimer NPs. (a) Co-culture of PLA-PEG/shellac dimer NPs with KPC and HPDE cells, showing good biocompatibility. (b) Mean fluorescent intensity of KPC cells after 24 h' co-culture with PLA-PEG/shellac and PLA-PEG-FA/shellac dimer NPs measured by flow cytometry. (c) Fluorescent confocal microscope images of KPC cells after 24 h' co-culture with PLA-PEG/shellac and PLA-PEG-FA/shellac dimer NPs. The concentrations of PLA-PEG/shellac and PLA-PEG-FA/shellac dimer NPs are the same of 5 μg/mL. The red signal represents NPs loaded with Nile Red, while the blue signal represents nuclei stained by DAPI. PLA-PEG/shellac dimer NPs are prepared using 10 mg/mL shellac and 10 mg/mL PLA with 2.5% PLA-PEG, while PLA-PEG-FA/shellac dimer NPs are prepared using 10 mg/mL shellac and 10 mg/mL PLA with 2.5% PLA-PEG-FA. ns, not significant. $^{***}P < 0.001$. Data are presented as mean ± standard deviation (SD) ($n = 3$).

NPs is up to 10 μg/mL, suggesting a good biocompatibility of the dimer NPs.

To investigate the performances of the dimer NPs as drug delivery vehicles, PLA-PEG-FA/shellac dimer NPs are easily prepared following the same procedure as PLA-PEG/shellac NPs, which benefit from the versatility of the NP preparation method. To characterize their cellular uptakes, PLA-PEG/shellac and PLA-PEG-FA/shellac dimer NPs are labeled by a fluorescent dye, Nile Red, and characterized by flow cytometry and fluorescent confocal microscopy. Since the FA group at the end of PLA-PEG supplements PLA-PEG-FA/shellac dimer NPs with a tumor-targeting function, the mean fluorescent intensity results confirm that PLA-PEG-FA/shellac dimer NPs have a better drug delivery performance than PLA-PEG/shellac dimer NPs, as shown in Fig. 6b. In addition, more fluorescent signals are directly observed under a fluorescent confocal microscope in KPC cells after 24 h' co-cultured with PLA-PEG-FA/shellac dimer NPs, as shown in Fig. 6c.

The strategy of preparing amphiphilic dimer NPs is unique and has several advantages: (i) The strategy is a green and scalable method simply based on one-step co-precipitation and self-assembly; (ii) NP size and shape could flexibly be tuned by changing the polymer concentration and concentration ratio, respectively; (iii) Surface functionality could simply be implemented to the NPs through the end of PLA-PEG; (iv) The method avoids any additional surface modification; (v) The strategy is versatile and applicable to different NPs. The developed PLA-PEG/shellac dimer NPs are biocompatible and amphiphilic and proved to be excellent colloidal surfactants and drug delivery vehicles.

Biocompatible amphiphilic PLA-PEG/shellac dimer NPs with tunable particle morphology and surface property are designed and prepared in a single step based on controlled co-precipitation and self-assembly. The performances of the amphiphilic dimer NPs as colloidal surfactants are investigated in detail. The amphiphilic dimer NPs, mimicking nonionic molecular surfactants, demonstrate excellent performances in stabilizing oil-in-water and water-in-oil emulsions. The flexible tuning of NP shape makes it facile to control the interfacial curvature and emulsion type. To demonstrate the versatility of the NP preparation method, temperature-responsive PLA-PNIPAM/shellac dimer NPs are prepared and emulsions stabilized by them show temperature-triggered response. In addition, the flexible tuning of NP shape and property makes it easy to enhance the cellular uptake to improve the drug delivery efficiency of PLA-PEG-FA dimer NPs. The developed strategy is thus green, scalable, facile and versatile, which provides a good platform for the design of dimer NPs with desired functionality and greatly facilitates their largescale production and widespread applications.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

CRediT authorship contribution statement

Xingqun Pu: Data curation, Investigation, Methodology, Writing – original draft. **Rongrong Liu:** Formal analysis, Investigation, Methodology, Writing – original draft. **Yuting Xie:** Investigation, Software. **Chenjing Yang:** Methodology, Software. **Jingyi Chen:** Formal analysis, Visualization. **Baoling Guo:** Conceptualization, Resources. **Chun-Xia Zhao:** Resources, Supervision. **Peng Zhao:** Resources, Supervision. **Jian Ruan:** Resources, Validation. **Fangfu Ye:** Resources, Visualization. **David A Weitz:** Project administration, Resources. **Dong Chen:** Conceptualization, Project administration, Resources, Validation, Writing – review & editing.

Acknowledgments

This work is supported by National Natural Science Foundation of China (No. 22278352), National Key Research and Development Program of China (No. 2021YFC3001100), Longyan City Science and Technology Plan Project (No. 2020LYF17043) and Longyan City Science and Technology Plan Project (No. 2020LYF17042), ARC Discovery Project (No. DP200101238) and NHMRC Investigator Grant (No. APP2008698). This work is also supported by the Harvard Materials Research Science and Engineering Center (No. DMR2011754).

Supplementary materials

Supplementary material associated with this article can be found, in the online version, at doi:10.1016/j.cclet.2024.109820.

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