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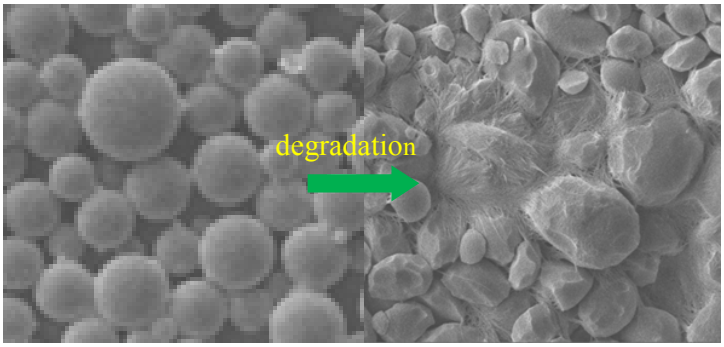

Degradable polymer microspheres were facilely fabricated by chitosan-based Pickering emulsion photopolymerization.

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ARTICLE

Fabrication of degradable polymer microspheres via pH-responsible chitosan-based Pickering emulsion photopolymerization

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Pickering emulsion stabilized by pH-reversible chitosan is developed to prepare degradable polymer microspheres by emulsion photopolymerization, where chitosan acts as a green and recyclable particulate emulsifier. The thiol-ene photopolymerization of trimethylolpropane tris(3-mercaptopropionate) and trimethylolpropane triacrylate is initiated by UV irradiation. Chitosan adsorbed at the surface of the microspheres can be recycled for polymerization at least three times. Ibuprofen (IBU) is loaded into the microspheres. The higher release temperature or pH value, the faster release rate and higher release extent of IBU from the microspheres are found. Meanwhile, the resulting microspheres exhibit a good degradability in 1 M NaOH aqueous solution, with a weight loss of about 90 wt% after 35 days. This study demonstrates a potential green and recyclable application of chitosan in fabrication of degradable polymer microspheres.

Introduction

Chitosan, which stems from the deacetylated derivative of chitin, is the second most abundant natural biopolymer found in nature only after cellulose. It's a natural linear polysaccharide with a molecular structure of β-(1-4)-linked D-glucosamine and N-acetyl-D-glucosamine units, where free amino and hydroxyl groups are along its backbone.[1,2] When pH is low, these amines are protonated, resulting in the dissolution of chitosan in acid solution. On the contrary, deprotonated amines cause chitosan insoluble at high pH values. Therefore, chitosan can easily undergo a pH-tunable sol-gel transition.[3] So far, most of the applications of chitosan still focus on the preparation of chitosan-based membranes, microcapsules, or other materials by grafting, functionalization, self-assembly, direct chemical or physical modification.[1,2,4-6] Few literature was reported to study the role of chitosan without any hydrophobic modification in stabilization of Pickering emulsion, which is the emulsion system stabilized by colloidal particles instead of surfactants.[7,8]

Pickering emulsions have aroused particular attention in recent years due to their significant advantages in contrast to traditional systems, such as good stabilization and low toxicity.[7-12] Pickering emulsions, especially pH-responsive systems, are of increasing interest to be studied in biomedical, pharmaceutical, cosmetic and coating. A large amount of literature has been reported to design pH-responsive Pickering emulsions based on pH-sensitive inorganic particles, organic polymer latexes.[13-15]

Stöver et al. designed a pH-responsive Pickering emulsion based on silica/potassium hydrogen phthalate, where stable emulsions only maintained at pH values between 3.5 and 5.5.[16] Fujii et al. had adopted nanocomposite microgels of poly(4-vinylpyridine)/silica to stabilize pH-responsive oil-in-water (O/W) Pickering emulsions, which could maintain stability at pH 8.0 and readily broke at pH 2.0.[17,18] Armes et al. prepared pH-responsive Pickering emulsions based on copolymerization polymer of poly(2-(diethylamino)ethyl methacrylate) latexes, where stable Pickering emulsions were prepared at pH 8.0 but demulsification occurred within seconds when the pH value decreased from 10 to 3.[19,20] Poly(N-isopropylacrylamide) based microgels are also an important thermo-responsive or pH-responsive emulsifiers to prepare responsive Pickering emulsions, these emulsifiers required the precise control of appropriate co-monomers.[21-23]

Unfortunately, these pH-responsive particulate emulsifiers mentioned above usually demanded significant synthesis effort or presented a certain degree of biological toxicity, which restricted the application of these emulsion systems in biotechnology, food science, environment protection. So, green and renewable bio-emulsifiers are particularly important in these fields.[24-27] Though the preparation of pH-responsive emulsifiers or emulsion systems was well documented, few

study was concentrated on the practical application of the pH-responsive emulsion system.

We have employed chitosan without any hydrophobic modification as a new and effective particulate emulsifier to prepare pH-reversible low and high internal phase Pickering emulsions for the first time.[3,28] Besides, we recently have successfully prepared pH-responsive O/W Pickering emulsions stabilized by natural polymer of lignin, and further recycled this emulsifier to prepare polystyrene microspheres by Pickering emulsion polymerization.[29] In the present work, pH-responsive chitosan-based Pickering emulsion was developed to synthesize degradable microspheres, and the cyclic utilization of chitosan in stabilization of Pickering emulsions and Pickering emulsion photopolymerization were studied in detail. The emulsion polymerization was carried out by UV irradiation of trimethylolpropane tris(3-mercaptopropionate) (trithiol) and trimethylolpropane triacrylate (TMPTA).

A schematic drawing of the preparation of degradable microspheres is presented in **Fig. 1**. The advantage of the microspheres or this method is: (i) the good controlled release behavior for loaded drug, ibuprofen (IBU) and a certain extent of degradability of microspheres, (ii) a new route for the green and renewable of chitosan in preparation of functional materials, and (iii) the versatile method for other reversible emulsifiers or emulsion systems. The major goal of this work is to develop a recycling route for photopolymerization base on pH-reversible Pickering emulsions. Through this method, we can prepare degradable microspheres more easily, economically and environmentally friendly. Drug delivery and degradation are investigated just as examples of properties for the obtained microspheres.

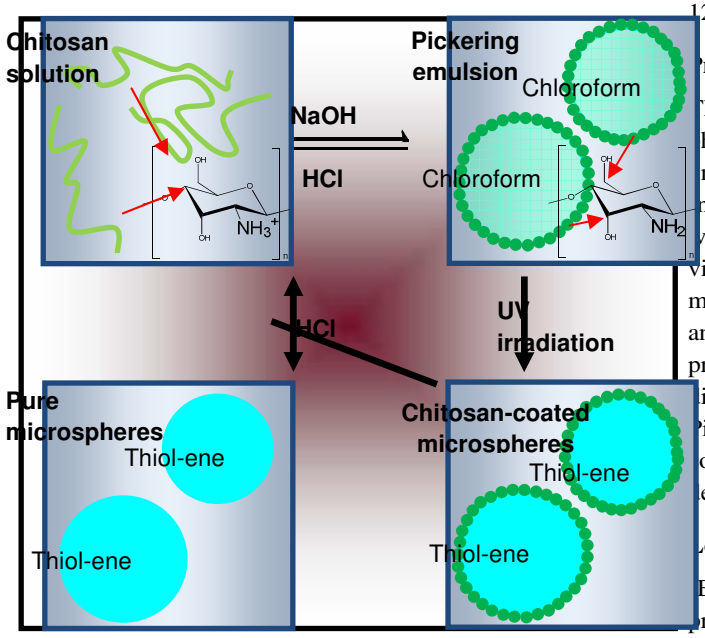

Fig. 1. Schematic representation of the recycling preparation of chitosan-coated microspheres and pure microspheres based on Pickering emulsion photopolymerization.

Experimental

Materials

Chitosan (degree of deacetylation □90 %, M_v = 60,000), trimethylolpropane tris(3-mercaptopropionate) (trithiol), trimethylolpropane triacrylate (TMPTA), the photoinitiator, a blend of diphenyl(2,4,6-trimethylbenzoyl)phosphine xide (TPO)/2-hydroxy-2-methylpropiophenone (Darocur 1173), ibuprofen (IBU), fluorescein isothiocyanate (FITC) were purchased from Sigma-Aldrich, and used without further purification. Chloroform, glacial acetic acid, dimethyl sulfoxide, sodium hydroxide (solid), and hydrochloric acid (Guangzhou Chemical Reagent Factory, China) were of analytical grade. Water used in all experiments was purified by deionization and filtration with a Millipore purification apparatus to the resistivity higher than 18.0 MΩ·cm.

Preparation of Pickering emulsions

A typical preparation procedure was based on our previously work.[3] Briefly, chitosan aqueous solutions (0.1, 0.5 or 1.0 wt%) were obtained by dissolving appropriate amount of chitosan powder in glacial acetic acid solution, where pH values were adjusted to about 4.1 by addition of 1 M NaOH or HCl aqueous solution. FITC-labelled chitosan were obtained by the reaction of chitosan solution and FITC solution (1 mg L^{-1} in DMSO) at 40 °C for 4 h, followed by precipitating at pH 9.5 to remove excess FITC.

Appropriate amounts of trithiol, TMPTA, photoinitiator were dissolved in chloroform, and chitosan solution at pH 6.7 was obtained by addition of NaOH or HCl solution. Then, 4 mL chitosan solution (0.1, 0.5 or 1.0 wt%) and 2 mL chloroform were homogenized to obtain chitosan-based Pickering emulsions with an IKA Ultra Turrax T25 basic instrument at 12,000 rpm for 2 min in an ice bath.

Preparation of microspheres

The resulting chitosan-based Pickering emulsions were used for photopolymerization to obtain chitosan-coated microspheres under a UV radiator apparatus (Intelli-ray 400, 400 W, Uvitron International, Inc. USA) for 10 min. The resulting microspheres were immersed into 1 M HCl solution for 2 h under mechanical vibration, and then purified by water washing to prepare pure microspheres. The supernatants produced during the dissolving and washing processes were adjusted to pH value of 9.5 to precipitate chitosan, followed by three centrifugation/re-dispersion processes to obtain clean chitosan solution. Then, Pickering emulsions stabilized by these recycling chitosan and corresponding microspheres were prepared as the same process described above.

Loading and release experiments

IBU-loaded chitosan-coated or pure microspheres were prepared as the procedure described above, except that certain amount of IBU was added into chloroform before homogenizing. All the supernatants produced during the washing process were collected, and the loading amount of IBU

inside the microspheres was estimated through the difference between the input amount and the amount in the supernatants produced during the washing process.

The IBU-loaded microspheres was dispersed into 20 mL PBS buffer solution (pH = 7.4 or 2.0), followed by transferred into a dialysis bag (M_w cut-off of 3500). Then, the dialysis bag was immersed into 380 mL PBS buffer solution under magnetic stirring, which was kept at different temperatures (20, 37 and 50 °C) using a thermostatic bath under continuously stirring of 200 rpm. After desired time intervals, 2.0 mL solution was taken out to analyze the IBU concentration. Following, this 2.0 mL solution was poured back into the PBS buffer solution. The release proceeded until the concentration of IBU in the PBS buffer solution remained unchanged. The concentration of IBU could be analyzed with UV-vis spectrophotometer through the calibration curve, which was established from standard solutions of IBU at pH = 7.4 or 2.0. The release profiles were averaged from three experiments.

Degradation studies

Microspheres of 0.2 g were added to NaOH solutions (0.1, 0.5 and 1 M). The solutions were kept at different temperatures. After desired time, the remaining microspheres were collected by three centrifugation/re-dispersion processes, followed by freeze drying. This process was carried out in triplicate and the percentage of weight loss was calculated from [(original mass – final mass)/original mass] × 100%.

Characterization

Pickering emulsion droplets were observed with an optical microscope (Carl Zeiss, German), and the average diameter was determined by a laser scattering particle size distribution analyser (Malvern Mastersizer 2000). The confocal micrographs were taken with a confocal laser scanning microscope (CLSM, Leica TCHITOSAN-SP2) with a 40 × objective. Chitosan was visualized by FITC-labelled polymer at excitation wavelength of 488 nm. Thermogravimetric analysis (TGA) was carried out with a NETZSCH TG 209F3 instrument. Samples were heated from 30 °C to 850 °C at a heating rate of 10 °C min^{-1} in nitrogen atmosphere. Scanning electron microscopy (SEM) was carried out with a Zeiss EVO 18 electron microscope equipped with a field emission electron gun. The samples were sputter-coated with gold prior to measurement. The quantification of IBU concentrations were evaluated by a Hitachi U-3010 UV-vis spectrophotometer at 223 nm.

Results and Discussion

Preparation of chitosan-based Pickering emulsions

It's well known that chitosan's amines are protonated at low pH value, but the amines are deprotonated at high pH value and chitosan nanoparticles are form, which can act a particulate emulsifier for Pickering emulsions. Actually, for the various oils with the different polarity and viscosity, O/W Pickering emulsions stabilized by chitosan exhibited good long-term stability for more than three months.[3] Herein, chloroform was selected as the model oil for Pickering emulsions.

The morphologies of Pickering emulsions stabilized by chitosan at pH 6.7 are shown in **Fig. 2**. The emulsion was O/W type, which was confirmed by droplet test.[3] Spherical emulsion droplets with good dispersibility could be observed. The mean droplet diameter (about 20 μm) of Pickering emulsion in Fig. 2a was obviously bigger than the diameters (about 10 μm) in Fig. 2b and 2c. The concentration of particulate emulsifier plays an important role in the stability and morphology of Pickering emulsions. At low chitosan concentration, there were not enough emulsifiers to stabilize small emulsion droplets, which had high specific surface area and required more emulsifiers. Thus, big emulsion droplets appeared. However, there was enough emulsifier to ensure small emulsion droplets at the chitosan concentration of 0.5 wt%. Excess chitosan (1.0 wt%) had no obvious effect on the size of emulsion droplets, which is accordance with the previous investigation.[3] So, the mean droplet diameter almost didn't have noticeable change at the chitosan concentration from 0.5 wt% to 1.0 wt%, but became smaller than the diameter at the concentration of 0.1 wt%.

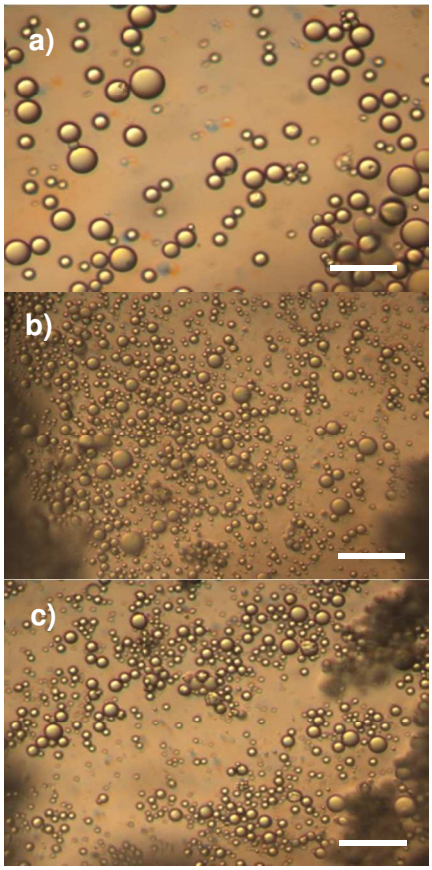

Fig. 2 Optical micrographs of chloroform-in-water Pickering emulsions prepared at chitosan concentrations of (a) 0.1 wt%, (b) 0.5 wt% and (c) 1.0 wt%. The oil to water volume ratio is 1:2. All scale bars represent 50 μm.

Preparation of microspheres

The colloidal particles adsorbed at oil-water interfaces need high energy to desorb from the interfaces, which impart unique advantage in stabilization of Pickering emulsions over traditional systems.[8,9,30] Thus, Pickering emulsion droplet can be used as a reaction vessel or robust template to fabricate microspheres, microcapsules, or other supracolloidal structures.[10,31-35] In this work, degradable microspheres were prepared by chitosan-based Pickering emulsion polymerization via UV irradiation of monomer (trithiol) and multifunctional acrylates (TMPTA). Compared to traditional thermopolymerization, photopolymerization has obvious advantages in fast curing speed (within several minutes, even a few seconds), easy control, insensitivity to oxygen.[36,37] What's more, the thiol-ene photopolymerization is very common and convenient, and various materials were obtained by thiol-ene photocuring under ambient temperature conditions.[38-40] Different amounts of trithiol and acrylate (1 and 2 in Fig. S1, respectively) were employed to produce the microspheres (**Table 1**). The morphology was observed by optical micrograph as shown in Fig. S2.

Table 1 Mass loss of chitosan-coated microspheres at different formulations.

	S1	S2	S3	S4	S5	S6
Trithiol (mL)	0.4	0.3	0.2	0.1	0.05	0.025
TMPTA (mL)	0.4	0.5	0.6	0.7	0.75	0.775
Mass loss[a] (%)	79.6	80.5	79.8	71.4	81.2	81.1

[a]Degradation was carried out at 37 °C for 7 days.

It's surprising that there were many microspheres binding together in Fig. S2a,b for entries S1 and S2 in Table 1, which suggested that the flocculation among emulsion droplets occurred in the polymerization process. On the contrary, well-defined and discrete microspheres were found in Fig. S2c-f (entries S3-S6 in Table 1, respectively). In all cases, photopolymerization proceeded steadily and no obvious phase separation was observed during the polymerization process. It could be supposed that excess trithiol (Fig. S2a,b) had a weak solubility in water and acted as a cross-linker to crosslink adjacent microspheres. However, all trithiol was responsible for the crosslinking and polymerization in individual emulsion droplet instead in Fig. S2b-d. If there is no special declaration, the microspheres refer to entry S4 in Table 1 with 0.1 mL trithiol and 0.7 mL TMPTA.

Then, the attempt of the removal of chitosan that already adsorbed on the surface of microspheres was conducted. Pure microspheres were obtained by dissolving the chitosan-coated microspheres in HCl solution to remove chitosan. **Fig. 3** shows the morphologies of chitosan-coated microspheres and pure microspheres for entry S4 (Table 1). The diameters of the two microspheres were roughly identical to the sizes of the corresponding emulsion droplets before polymerization. The comparable diameters, combining the phenomenon of no phase separation during the polymerization process, indicated that chitosan-based Pickering emulsion provided a really stable reaction vessel to produce microspheres.

Rough surface of chitosan-coated microspheres were presented in Fig. 3a (more obvious at a high magnification image in Fig. $3a_2$), but the surface of the pure microsphere in Fig. $3b_2$ was clean and smooth after chitosan dissolving in HCl solution. Therefore, the aggregation small particles appeared on the surface of the microsphere in Fig. $3a_2$ should be the particulate emulsifier of chitosan. The presence of N element in EDS analyse (Fig. $3a_3$) and absence of this element in Fig. $3b_3$ demonstrated that chitosan existed on the surface of chitosan-coated microspheres, and chitosan was successfully removed after HCl washing. Besides, this phenomenon further suggested that the chitosan adsorbed at the oil-water interfaces prevented droplet coalescence during the photopolymerization process, and chitosan could be easily removed by dissolving in acidic condition.

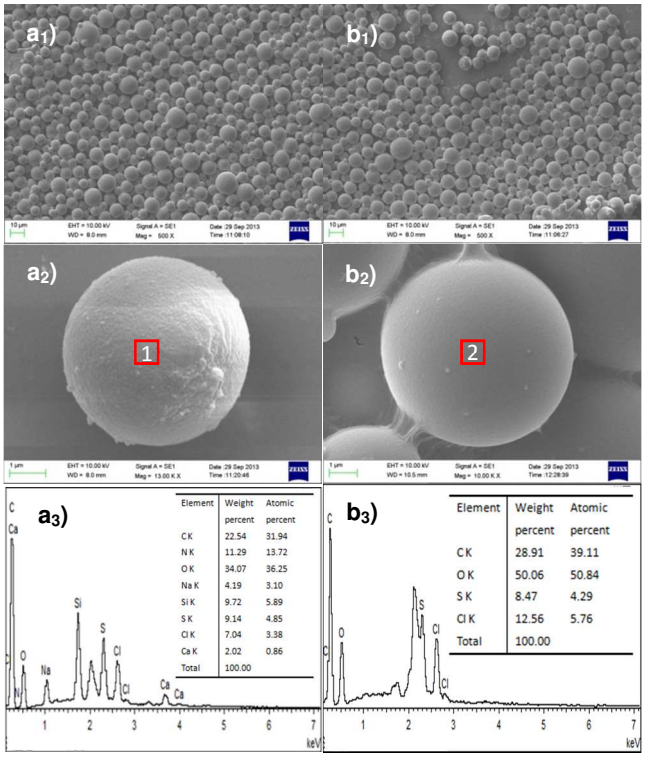

Fig. 3 SEM images of chitosan-coated microspheres (a_1, a_2) and pure microspheres (b_1, b_2). EDS spectra at (a_3) surface area 1 of the microsphere in a_2 and (b_3) surface area 2 of the microsphere in b_2.

To further investigate the surface structure of chitosan-coated microspheres, FITC-labelled chitosan acted as emulsifiers to prepare Pickering emulsions and microspheres. The microspheres before and after HCl washing are shown in **Fig. 4**a and 4b, respectively. It is noted that green fluorescence almost only existed at the surface of microspheres in Fig. 4a, and the fluorescence appeared in the surrounding medium in Fig. 4b. This observation is well in accordance with the SEM

experiments (Fig. 3). However, irregular microspheres appeared in Fig. 4a, which was a little different from the morphologies in Fig. 3a. This different may be due to the shorter photopolymerization time of Pickering emulsion stabilized by FITC-labelled chitosan, where the shorter time was employed in order to avoid the quenching of FITC under UV irradiation. Meanwhile, chitosan can't be labelled by FITC uniformly, which makes the fluorescence with polydispersity in the confocal microscopy images.

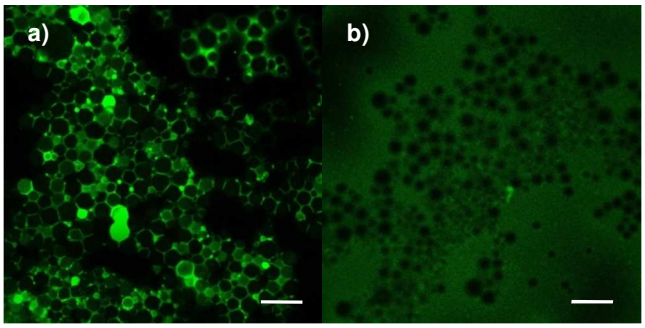

Fig. 4. Confocal microscopy of the microspheres before (a) and after (b) HCl washing. Chitosan was labelled by FITC. All scale bars represent 25 μm.

The content of chitosan in chitosan-coated microspheres was roughly estimated by TGA analysis (**Fig. 5**). The residues of chitosan, chitosan-coated microspheres and pure microspheres above 800 °C were about 39.4, 11.1, and 6.6 wt%, respectively. So, the calculated content of chitosan in chitosan-coated microspheres was about 13.7 wt%.

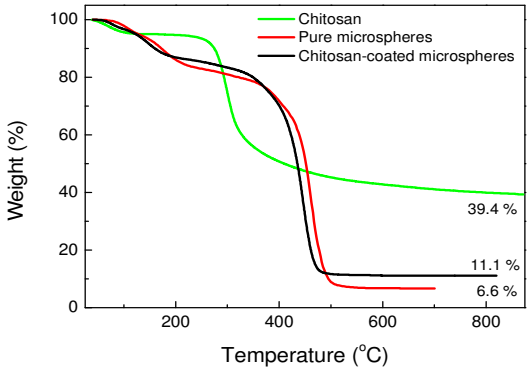

Fig. 5. TGA curves of chitosan, pure microspheres and chitosan-coated microspheres.

Table 2 Mean diameters of chitosan-coated microspheres at different cycling numbers.

	Chitosan concentration(wt%)	Mean diameters (μm)		
		1	2	3
S7	0.1	21.2	37.3	40.5
S4	0.5	9.7	10.8	19.3
S8	1.0	9.5	15.4	13.8

Recycling route for photopolymerization

The role of pH-responsive chitosan in the preparation of microspheres was investigated. Chitosan was recycled by immersing the chitosan-coated microspheres in HCl solution, followed by precipitating at pH 9.5 and three centrifugation/re-dispersion processes, as shown in Fig. 1. The repeatability of the chitosan-based emulsion photopolymerization was conducted at different chitosan concentrations of 0.1, 0.5 and 1.0 wt% (**Table 2**). SEM morphologies of three recycle emulsion polymerization processes are depicted in **Fig. 6**. When chitosan concentration was 0.1 wt%, irregular microspheres or microsphere aggregations were found after two recycles of emulsion polymerization (Fig. 6a_2 and a_3). However, well-defined microspheres were clearly presented in Fig. 6b and 6c under all three cycles. The mean diameters of microspheres are presented in Table 2. The diameter obviously increased with increasing the recycle times at the chitosan concentration of 0.1 wt%, but the size of the final microspheres marginally increased at the concentration of 0.5 and 1.0 wt%. The chitosan concentration is crucial for the stability and droplet diameter of Pickering emulsion, as a result, play an important part in controlling the morphologies and diameters of microspheres. During the recycle of chitosan, a slight loss of chitosan appeared at the route of dissolving, precipitating, and centrifugation/re-dispersion processes. As discussed above, low chitosan concentration would form relatively big emulsion droplets and correspondingly result in big microspheres. At chitosan centration of 0.1 wt%, there were not enough chitosan that could effectively stabilize Pickering emulsions after one recycle. Consequently, the emulsion droplets easily trended to break up and polymerization among droplets were not rare to form microsphere aggregations. At chitosan centration of 0.5 wt%, there were still sufficient emulsifiers to form stable Pickering emulsions, although a little loss of chitosan after three recycles. Further increasing chitosan concentration actually generated no additional effect on morphologies and sizes of final microspheres. Therefore, the chitosan concentration was fixed at 0.5 wt% for the following microsphere preparation processes.

The technological process of photopolymerization of chitosan-based Pickering emulsions is a simple and effective approach for preparation of various functional materials. Pickering emulsion systems stabilized by chitosan could also be applied in other fields of industrialization, for example polystyrene synthesis, not shown in this work. Compared to lignin used in our previously work,[29] chitosan has unique advantages in some fields, especially in biomedical field due to the properties of biocompatibility and biodegradability of chitosan.

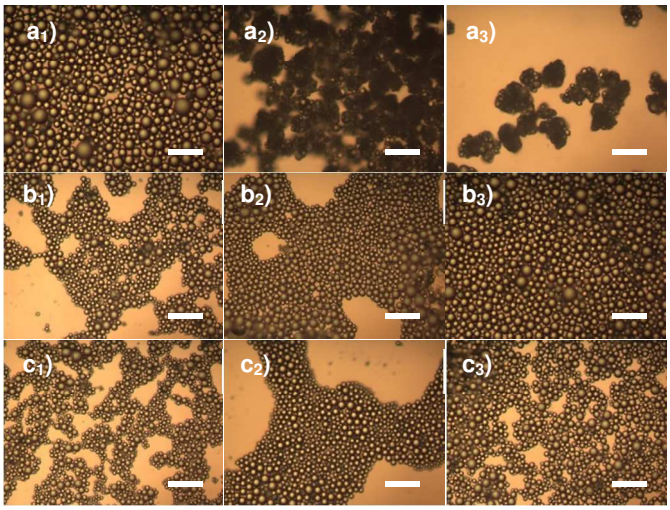

Fig. 6. Optical micrographs of the microspheres prepared at chitosan concentrations of (a) 0.1 wt%, (b) 0.5 wt% and (c) 1.0 wt%. The numbers, 1-3 represent the cycle times. All scale bars are 50 μm.

Controlled release of IBU from microspheres

The chitosan-coated and pure microspheres were used to study the drug release behavior. IBU delivery and release has been widely studied.[41,42] In this study, IBU was also chosen as a model drug to load into the microspheres. The encapsulation efficiency of IBU in the microspheres was determined by the difference between the total amount and the amount in the supernatants during the washing process. The encapsulation efficiency was almost 100 % for the chitosan-coated microspheres. For the pure microspheres, the encapsulation efficiency had a very slight decrease due to the washing processes with IBU saturated HCl/water. The encapsulation efficiency is higher than that of the microspheres prepared in our previous work.[43]

Fig. 7 shows the IBU release from the chitosan-coated and pure microspheres as a function of time at pH 7.4 and 2.0 under 37 °C. All microspheres followed a similar release tendency: The initial stage of fast release in about 65 min, and the second stage of slow release to a platform (65-130 min). In contrast to the IBU release at pH 2.0 (a maximum release of 33.9 %), the release was greatly faster at pH 7.4 and the maximum release amount reached 58.1 %. It's well known that IBU molecule exhibits a better solubility at pH 7.4 than at pH 2.0, which results in the significant difference of IBU release at different pH values. To our surprise, the IBU release from the chitosan-coated microspheres and pure microspheres almost displayed the same controlled release behavior. Presumably, the big gap among the chitosan aggregations, which adsorbed on the surface of the chitosan-coated microspheres, provided almost no obstacle to the channel of IBU release.

Then, the effect of temperature (20, 37 and 50 °C) on the IBU release at pH 7.4 was investigated as shown in **Fig. 8**. The IBU release rates at 37 and 50 °C were obviously faster than that at 20 °C, and the release rate at 50 °C was a little faster than that at 37 °C. Besides, the total release amount gradually increased slightly with raising temperature, and the release amounts were57.8, 58.1 and 58.9% at 20, 37 and 50 °C, respectively. The increment of release rate and amount may be due to the slight increase of IBU solubility in aqueous solutions at higher temperature. The IBU release suggested that the release rate can be controlled by tuning release temperature or ambient medium like pH value.

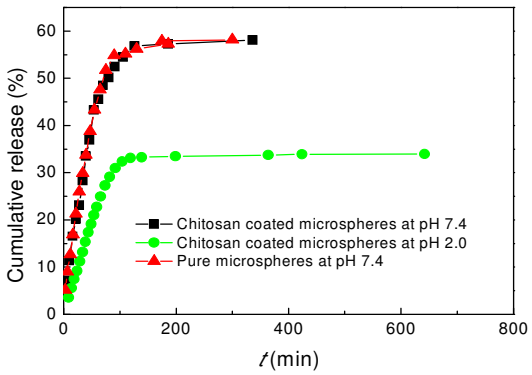

Fig. 7. IBU release from the microspheres at pH 7.4 and 2.0.

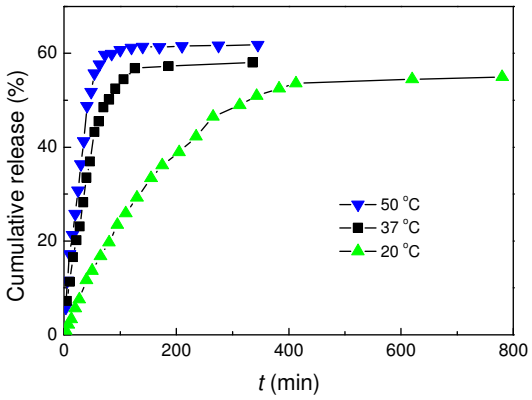

Fig. 8. IBU release from chitosan-coated microspheres at pH 7.4 at different temperatures.

Degradation studies

Degradation is important to polymeric spheres for drug delivery. Because of plenty of ester linkages (R-COO-R') in the microspheres introducing by trithiol and TMPTA, the resulting microspheres should degrade in alkaline condition. Degradation studies were initially performed at 1.0 M NaOH aqueous solution under 37 °C (Table 1). In this case, degradations were carried out for 7 days and the degradation extent displayed similar to each other in the range of 71-82 % mass loss, regardless of the compositions of microspheres. Actually, the degradation extent was mainly determined by the amount of ester linkages in microspheres, where the total amount of ester linkages was almost no change in different entries in Table 1.

Next, degradation studies were performed at different NaOH aqueous solutions and temperature, as shown in **Table 3**. With increasing both of the concentration of NaOH solutions

and the degradation temperature, the degradation rate greatly increased as expected. However, in contrast to degradation extent at 37 °C, the extent at 50 °C in 1 M NaOH solution was little increase, indicating that temperature plays a weak role in speeding up the degradation rate at high concentration of NaOH solution.

Table 3 Mass loss of pure microspheres at different NaOH concentrations for 7 days.

Temperature (°C)	Mass loss (%)		
	0.1 M	0.5 M	1 M
20	11.6	23.8	40.0
37	15.0	27.3	71.4
50	27.8	70.4	72.4

Fig. 9 shows the mass loss of pure microspheres in 1 M NaOH at 37 °C as a function of time. The degradation rate was initially very fast and then gradually decreased until a mass loss plateau of about 90 % was reached. The degradation extent of the microspheres in this work was smaller than that of the scaffold materials consisted of the same monomers in literature,[37] due to the high porosity of scaffolds where NaOH solution was more easily to permeate into the interior section.

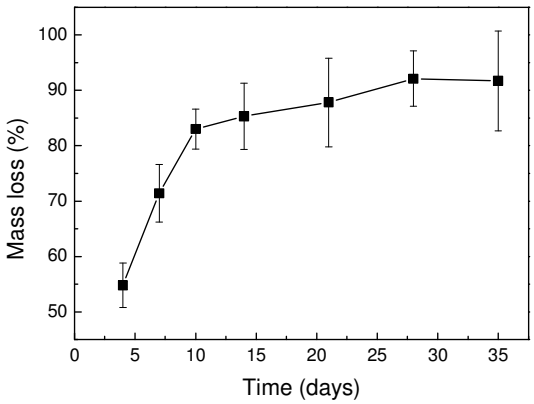

Fig. 9 Mass loss of pure microspheres in 1 M NaOH at 37 °C as a function of time. Error bars represent standard deviation of the mean (n = 3).

The morphologies of pure microspheres degraded for 7 days in 0.1 or 1 M NaOH solution are shown in **Fig. 10**. In contrast to Fig. 3, the images in Fig. 10 displayed a completely different morphology. Part of polymer microspheres of thiol-ene was corroded off by the NaOH solution; there even appeared polymer fibers in Fig. 10b. The degradation extent in 1 M NaOH solution was higher than that in 0.1 M NaOH solution. The higher contents of Na and O and lower content of C for the former from Fig. $10b_3$ and $10a_3$ also suggested the higher degradation extent in 1 M NaOH solution. All the results demonstrated that we had successfully prepare degradable microspheres through Pickering emulsion photopolymerization, and the degradation extent and rate could be adjusted by the concentration of NaOH solutions and the degradation temperature. However, the degradation at harsh conditions of 0.1 to 1 M NaOH will not happen in the human body. The microspheres had a certain extent of degradability, instead of biodegradability. Maybe this degradable behavior can make these microspheres find applications in other situations but in the body.

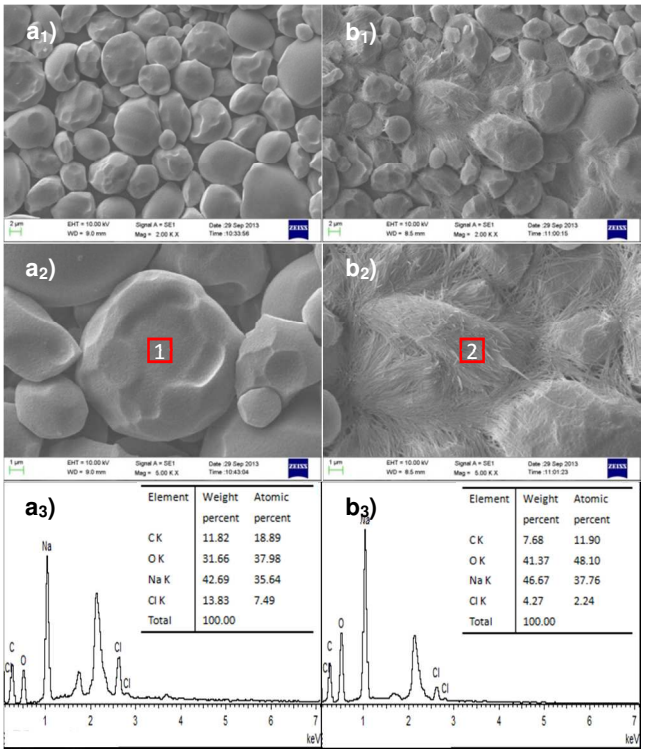

Fig. 10. SEM images of pure microspheres incubated in 0.1 M NaOH (a_1, a_2) and 1 M NaOH (b_1, b_2) at 37 °C for 7 days. EDS spectra at (a_3) surface area 1 of the microsphere in a_2 and (b_3) surface area 2 of the microsphere in b_2.

Conclusions

In summary, pH-reversible chitosan based Pickering emulsion was demonstrated in the recycling preparation of degradable microspheres under UV thiol-ene photopolymerization. The pH-reversibility of chitosan endowed it to be used for recycles in emulsion polymerization at least three times. Pure microspheres were obtained by dissolving the chitosan-coated microspheres in acidic solution to remove chitosan. Both microspheres showed controlled release behavior of IBU and a certain extent of degradability in alkaline solution, which could be tuned by the pH value and temperature of the surrounding medium. The proposed approach for preparation of degradable microspheres based on Pickering emulsion stabilized by pH-responsive chitosan expands the application of a wide range of reversible emulsifiers or emulsion systems in green economy or environment protection.

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Notes and references

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† Footnotes should appear here. These might include comments relevant to but not central to the matter under discussion, limited experimental and spectral data, and crystallographic data.
Electronic Supplementary Information (ESI) available: Structural formula, Optical micrographs. See DOI: 10.1039/b000000x/

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