Optimization and characterization of high pressure homogenization produced chemically modified starch nanoparticles

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Abstract Chemically modified starch (RS4) nanoparticles were synthesized through homogenization and water-in-oil mini-emulsion cross-linking. Homogenization was optimized with regard to z-average diameter by using a three-factor-three-level Box–Behnken design. Homogenization pressure (X_1), oil/water ratio (X_2), and surfactant (X_3) were selected as independent variables, whereas z-average diameter was considered as a dependent variable. The following optimum preparation conditions were obtained to achieve the minimum average size of these nanoparticles: 50 MPa homogenization pressure, 10:1 oil/water ratio, and 2 g surfactant amount, when the predicted z-average diameter was 303.6 nm. The physicochemical properties of these nanoparticles were also determined. Dynamic light scattering experiments revealed that RS4 nanoparticles measuring a PDI of 0.380 and an average size of approximately 300 nm, which was very close to the predicted z-average diameter (303.6 nm). The absolute value of zeta potential of RS4 nanoparticles (39.7 mV) was higher than RS4 (32.4 mV), with strengthened swelling power. X-ray diffraction results revealed that homogenization induced a disruption in crystalline structure of RS4 nanoparticles led to amorphous or low-crystallinity. Results of stability analysis showed that RS4

nanosuspensions (particle size) had good stability at 30 °C over 24 h.

Keywords Homogenization · Mini-emulsion cross-linking · Box–Behnken design · RS4 nanoparticle · Physicochemical properties

Introduction

Protecting drugs against degradation is important. Nano-sized drug carriers are commonly used in drug delivery systems because their small size allows them to permeate through biological barriers (Xu et al. 2014). Starch is a naturally occurring polymer that features bio-compatibility, biodegradability, and bio-adhesion. It is a polysaccharide that contains amylose and amylopectin (Pang et al. 2011). Previous reports on starch nanoparticles derived from rice, cassava, and corn indicated that nano-sized starches can be used as fillers to improve the mechanical and barrier properties of biocomposites (Chivrac et al. 2009; Le Corre et al. 2010). However, the development of nanostructures from the resistant starch RS4 has not been described in the literature. Given its specific characteristics, RS4 can be exploited as an alternative polysaccharide in nanocomposite development (Thys et al. 2008). RS4 has been recently targeted for use in food products (Fuentes-Zaragoza et al. 2011). RS4 is resistant to digestion because of chemical modification. This paper presents the preparation of RS4 nanoparticles.

Earlier works obtained drug-loaded nanoparticles through drug adsorption on the particle surface (Hernandez et al. 2012). Different polymerization techniques have been used to incorporate drugs into nanoparticles. Many administration routes have been investigated for

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nanoparticle production; these routes include emulsion cross-linking, acid or enzyme hydrolysis of native starch granules, supercritical fluid extraction, solvent evaporation, complex coacervation, and spray drying (Liu et al. 2005). However, the size distribution of nanoparticles prepared using these methods is broad, which results in poor targeting and low bioavailability. In addition, these methods only physically bind drugs onto the nanoparticle. This fact limits the controlled release properties of nanoparticles and increases the possibility of an uncontrolled desorption of the drug from the nanoparticle surface under certain environmental influences.

Many physical emulsification techniques, such as high shear emulsification, sonication, and high pressure homogenization, can be used to prepare miniemulsions. High pressure homogenization has been developed recently as a highly efficient emulsification technique. Compared with ultrasonication and high shear emulsification, high pressure homogenization can produce smaller droplets and better homogeneity in emulsions. The productivity of high pressure homogenization is the best among the above-mentioned emulsification methods (Asua 2002). Combining high pressure homogenization and miniemulsion cross-linking reaction may yield starch submicron particles in emulsion droplets.

Box–Behnken method with a response surface methodology (RSM) design is used to optimize output surface responses influenced by various independent input parameters (Ding et al. 2016a; Prabhu et al. 2017). Compared with other statistical designs, Box–Behnken design contains three levels and requires few experiments; consequently, this design involves non-laborious experimental work, consumes low amounts of reagents, and easily contracts or expands in the experimental domain (Espadabelido et al. 2016).

The present study aimed to develop a novel emulsion cross-linking technique involving high pressure homogenization to prepare small RS4 nanoparticles. The homogenization power, oil/water ratio, and surfactant amount were optimized to achieve the most favorable size of RS4 nanoparticles by using a Box–Behnken factorial design. Finally, the particle size, polydispersity, zeta potential, crystal structure of RS4 nanoparticles and stability analysis of RS4 nanosuspensions were investigated.

Materials and methods

Materials and chemicals

RS4 was purchased from National Starch (USA). N,N'-methylenebisacrylamide (MBAA), $K_2S_2O_8$, $NaHSO_3$, acetic acid, Tween-80, Span-80, potassium hydroxide,

potassium persulfate, sodium bisulfite were provided by Chongqing Chemical Company (Chongqing, China). Amylopectin, amylose from potato starch, pancreatin (526U/mg) from hog pancreas and pepsin (526 U/mg) from porcine gastric mucosa were purchased from Sigma (USA). All these reagents were analytical reagent grade and used without further purification.

Homogenization-assisted preparation of RS4 nanoparticles

W/o mini-emulsion technique, which was previously applied to synthesize nano-size and micro-size particles (Ding et al. 2016b, c), was used to prepare the nanoparticles. The MBAA was used as cross-linking agent while $K_2S_2O_8$ and $NaHSO_3$ were used as evocating agent. At the emulsification process, a high-pressure homogenizer was applied, hence, the average size of the dispersed droplets was reduced to a great extent. Figure 1 shows the flowchart for preparation of the RS4 nanoparticles. Briefly, RS4 (0.05 g) was first dissolved in a potassium hydroxide solution (10 mL, 2 mol/L) with stirring for 2 h at 45 °C and added with 0.05 g of MBAA, 0.027 g of $K_2S_2O_8$, and 0.104 g of $NaHSO_3$ to form the aqueous phase. Subsequently, the emulsifier was mixed using Span-80 and Tween-80 at 84:16 and was dissolved in cyclohexane at 45 °C (according to Table 1). Then, the mixture was stirred to form the organic phase. The aqueous phase was poured into the organic phase to prepare the coarse emulsion. The coarse emulsion was subsequently homogenized in a high-pressure homogenizer (ATS[®] AH-100D, BVI, Canada) at pressures ranging from 20 to 60 MPa (according to Table 1) for 3 min. In the end, after 12 h cross-linking and solidification reaction at 25 °C with constant stirring (250 r/min), the RS4 submicron particles were collected.

In order to obtain the RS4 nanoparticles from the mini-emulsion, 15% acetic acid was added to the mini-emulsion, and the mixture was centrifuged at 3000g (ALPHA1-4LSC, Christ, Germany) for 30 min. The nanoparticles obtained after centrifugation were further purified using acetone and finally washing with water and followed by spray drying (GPW120-II, China). The dry samples were packed in Ziploc bags and stored in a dryer for the next study.

Optimization using the Box–Behnken design

In this study, a three-factor, three-level Box–Behnken design was designed. These independent factors were studied at low, middle and high levels coded as −1, 0, and 1, respectively. The optimization was performed using three independent variables: homogenization pressure (X_1), oil/water ratio (X_2), and surfactant amount (X_3). The result

Fig. 1 Flow chart of the RS4 nanoparticle preparation

for the average size (Y) was considered as the response variable. The whole experimental design matrix is shown in Table 1.

Study of the physicochemical and functional properties

Average particle size distribution

The polydispersity index (PdI) and average size of the RS4 nanoparticles were analyzed by a Zetasizer Nano ZS (Malvern, England). RS4 nanoparticles were diluted in DI water and measured by the Zetasizer Nano ZS at 25 °C (Ding and Kan 2016). The PdI and weighted average particle size of the average of three mean measurements were recorded.

Zeta potential

The sample suspensions (pH 7.0) prepared by diluted samples in DI water (0.01%, w/v), and measured the zeta potential by laser doppler velocimetry using a Zetasizer Nano ZS (Malvern, England), following the method reported by Mahmoudi Najafi et al. (2016). For each sample, the zeta potential was measured three times, and each measurement was performed for at least 12 runs.

Stability analysis of RS4 nanosuspensions

The physical stabilities of the RS4 nanosuspensions (0.1%) were carried out in accordance with the method described by Patel et al. (2016). The RS4 nanosuspensions were obtained by dispersing 10 mg RS4 nanoparticles in 10 mL water medium, then were stored for 0, 12, 24, 48, 72 h at 30 °C. The size of the RS4 nanosuspensions was determined by a Zetasizer Nano ZS (Malvern, England). RS4 nanosuspensions were sonicated for 2 min before the size measurements.

Swelling studies

Swelling studies of the samples were measured by following the method of Ding and Kan (2016). Dried samples (200 mg) were dispersed in 30 mL of DI water for 30 min. The suspension was placed in a water bath with continuous stirring (300 r/min) at 85 °C, then was centrifuged (ALPHA1-4LSC, Christ, Germany) at 4000g for 25 min. Finally, the supernatant was removed and the residue was obtained. The changes in the weight of the samples was measured and recorded. Using the formula below, the swelling percentage of the samples was determined:

$$\text{Swelling (\%)} = \frac{(\text{Final weight after swelling} - \text{Initial weight}) \text{ of the samples}}{\text{Initial weight of samples}} \times 100$$

Table 1 Three variables and full factorial central composite design in coded and natural units with these obtained responses

Factors		Units	Symbols	Level of factors				
				− 1	0	1		
Homogenization pressure		MPa	X_1	30	40	50		
Oil/water			X_2	8:1	10:1	12:1		
Surfactant amount		g	X_3	1	2	3		
Std. order	X_1		X_2		X_3		Z-Ave (d.nm)	
	Coded	Uncoded	Coded	Uncoded	Coded	Uncoded	Experimental	Predicted
1	− 1	30	− 1	8:1	0	2	431.5	431.9
2	1	50	− 1	8:1	0	2	348.2	347.6
3	− 1	30	1	12:1	0	2	384.2	384.8
4	1	50	1	12:1	0	2	379.2	378.8
5	− 1	30	0	10:1	− 1	1	450.9	450.4
6	1	50	0	10:1	− 1	1	348.8	349.2
7	− 1	30	0	10:1	1	3	401.5	401.1
8	1	50	0	10:1	1	3	411.4	412.0
9	0	40	− 1	8:1	− 1	1	462.9	463.0
10	0	40	1	12:1	− 1	1	454.6	454.6
11	0	40	− 1	8:1	1	3	469.3	469.3
12	0	40	1	12:1	1	3	461.9	461.8
13	0	40	0	10:1	0	2	333.0	334.6
14	0	40	0	10:1	0	2	338.5	334.6
15	0	40	0	10:1	0	2	334.6	334.6
16	0	40	0	10:1	0	2	331.7	334.6
17	0	40	0	10:1	0	2	335.2	334.6

X-ray diffraction (XRD)

Amorphous/crystalline structure of dried RS4 and RS4 nanoparticles was examined by an X-ray diffraction (PERSEE, China) as described by Ding and Kan (2016). The 2-theta (2θ) temperature range from 10° to 60° at intervals of $0.02^\circ/\text{s}$ was used.

Statistical analysis

All experiments were conducted in duplicate. The data were analyzed statistically using analysis of variance (ANOVA) using Minitab Release 14. Mean values were considered significantly different when $p < 0.05$.

Results and discussion

Box–Behnken design analysis

Model fitting and statistical analysis

The response of RS4 nanoparticles formation, as a function of homogenization pressure, oil/water ratio, and surfactant amount was evaluated in a central composite design. The design matrix and the corresponding results with experimental and predicted responses of 17 runs obtained by Box–Behnken design are presented in Table 1. The second-order polynomial equation describing the relationship between the significant variables and the z-average diameter of RS4 nanoparticles is given below:

Fig. 2 2D and 3D contour plots showing the effects of (A, a) homogenization pressure and oil/water ratio, (B, b) homogenization pressure and surfactant, and (C, c) oil/water ratio and surfactant on the size of RS4 nanoparticles

Fig. 3 **a** The average size distribution of RS4 nanoparticle; **b** zeta potential of RS4 and RS4 nanoparticle. Values in Fig. 3 followed by different lowercase letters in superscripts are significantly different from each other according to Duncan's multiple range tests ($p < 0.05$)

$$Y = 334.6 - 22.56X_1 - 4.00X_2 + 3.36X_3 + 19.57X_1X_2 + 28.00X_1X_3 + 0.22X_2X_3 - 3.93X_1^2 + 55.1X_2^2 + 72.48X_3^2 \quad (1)$$

where Y is the z-average diameter of RS4 nanoparticles; and X_1 , X_2 , and X_3 are the coded terms for homogenization pressure, oil/water ratio, and surfactant amount, respectively.

The p value indicates the improvement of model due to the additional terms while demonstrating the effect of the individual controlled factor on the model (Swamy and Muthukumarappan 2016). The F -value should be high while the p value should be low for a model to be significant (Prabhu et al. 2017). The adjusted model has a high value of F (1248.41), which indicated that the adjusted model has a highly significant value. Also, the adjusted model has a low value of p ($p < 0.0001$) that confirmed

Fig. 4 X-ray diffraction patterns of RS4 and RS4 nanoparticles

that the adjusted model was significant. The fairly high values of R^2 (0.9994) and the adjusted correlation coefficient ($\text{Adj-}R^2 = 0.9986$) also clearly demonstrated that the model was statistically significant. The value of $\text{C.V.} = 0.51\%$ showed that the accuracy and general availability of the polynomial model were adequate. However, the lack of fit of the adjusted model was 0.9562, which has no significance, thus, suggesting that the obtained model is an appropriate model for optimization the RS4 nanoparticle formation. The p values of the linear coefficients X_1 , X_2 , and X_3 , cross product coefficients X_1X_2 and X_1X_3 , and quadratic coefficients X_1^2 , X_2^2 , and X_3^2 were all lower than 0.01, hence demonstrating that they were the most significant factors among the factors influencing the response, whereas the other term coefficients were insignificant ($p > 0.05$).

2D contours and 3D response surface plots

To study further the influences of the independent variables and their interactions on the response, 3D response surface plots and 2D contour plots were employed. The results are shown in Fig. 2. Each 3D response surface plots and 2D contour plots figure shows the effects of two variables on the z-average diameter, whereas the other one was fixed at the fixed levels. Different shapes of the contour plots indicate different interactions between the variables; a circular contour plot implies that the interactions between the corresponding variables are negligible, whereas an elliptical contour plot means otherwise (Chen et al. 2012). As shown in these figures, X_1X_2 and X_1X_3 significantly correlated, whereas X_2X_3 showed no significant interaction. Figure 2A, a shows the combined effect of homogenization pressure and oil/water ratio on the particle size of RS4 nanoparticles at a constant surfactant amount. Figure 2B, b shows the interactive effect

Fig. 5 a Swelling of RS4 and RS4 nanoparticles; b the variety of the average size of RS4 nanoparticle with different time in aqueous. Values in Fig. 5 followed by different lowercase letters in superscripts are significantly different from each other according to Duncan's multiple range tests ($p < 0.05$)

of homogenization pressure and surfactant on particle size at constant oil/water ratio. Figure 2C, c shows the interactive influence of oil/water ratio and surfactant on the particle size at constant homogenization pressure. As shown in Fig. 2, the particle size of RS4 nanoparticles decreased with the increase in homogenization pressure and oil/water ratio, homogenization pressure and surfactant, oil/water ratio and surfactant as earlier. However, a rising trend was noted with the increased homogenization pressure and oil/water ratio, homogenization pressure and surfactant, oil/water ratio and surfactant in the experimental range.

As shown in Fig. 2A, a, B, b, the particle size decreased with the increase of homogenization pressure. Collision between droplets, which accelerated droplet breaking, became stronger with increasing pressure. Homogenization pressures lower than 30 MPa were not enough to break droplets into small and uniform emulsions and resulted in

large RS4 nanoparticles (Ding et al. 2016b, c; Lamprecht et al. 2000).

As shown in Fig. 2A, a, C, c, the particle size initially decreased and then increased with the increase of oil/water ratio. Shi et al. (2011) found that the decrease size may be due to the fact that when the water phase volume is decreased, higher power input during the emulsification process is needed to reduce the droplet size. Furthermore, at higher oil/water ratios of emulsion, the possibility of complete homogenization of the emulsion increases when higher oil/water ratios are used. In this situation relatively smaller RS4 nanoparticles will be produced compared to the ones formed from lower oil/water ratios (Antonietti and Landfester 2002).

As shown in Fig. 2B, b, C, c, the particle size initially decreased and then increased with the increase of surfactant amount. The lowest particle size was obtained when the surfactant amount was 2 g. “The optimal amount” theory provides the possible explanation for this phenomenon. When the surfactant amount is insufficient to coat the entire surface area of the droplets after homogenization, the droplets aggregate with each other to reduce the surface area (Niemann and Sundmacher 2010). By contrast, when the surfactant amount in the oil phase is excessive, the free emulsifier molecules formed within the emulsion ultimately adhere to the droplets and become covered by the excess amount of surfactant. Both of the above scenarios lead to the absorption and dispersion of emulsification energy. Antonietti and Landfester (2002) and Asua (2002) reported similar observations regarding the effect of surfactant concentration on nanoparticles.

Verification of predictive model

After carrying out the detailed experimental design to optimize the three independent variables in order to get the small average size of RS4 nanoparticles, it can be concluded that the optimum process conditions are as follows: homogenization pressure of 50 MPa, oil/water ratio of 10:1; and surfactant amount of 2 g. Using these values, we will achieve the minimized average size (303.6 nm) of the RS4 nanoparticles. Under the actual optimum extraction conditions, the experimental z-average diameter of the RS4 nanoparticles was 318.3 nm, which agreed with the predicted value. These results suggest that the response model can be used to optimize the preparation of RS4 nanoparticles (Ding et al. 2016a, b, c).

Characterization of RS4 nanoparticles

We prepared RS4 nanoparticle using RS4 concentration of 0.05 g/10 mL, oil/water ratio of 10:1, surfactant amount of

2 g, homogenization pressure of 50 MPa and homogenization time of 3 min.

Particle size and zeta potential analysis

The size distribution of RS4 nanoparticles is presented in Fig. 3A. From Fig. 3A, homogenization-treated RS4 resulted in an average diameter of 318.3 nm and a PDI of 0.380. These PDI values indicate that the RS4 nanoparticles had a narrow size distribution and homogeneity. The high size reduction observed for homogenization may be associated with cavitation forces because the successive release of starch fragments from the granule surface results in a small particle size. The particle size reduction works by increasing the surface area.

As can be seen in Fig. 3B, the zeta potential measurements showed that RS4 and RS4 nanoparticles were consistently negative, and there were difference in zeta potential between the RS4 and RS4 nanoparticles. The absolute value of zeta potential of RS4 nanoparticles (39.7 mV) was higher than RS4 (32.4 mV).

XRD analysis

The XRD results of RS4 and RS4 nanoparticles are shown in Fig. 4. RS4 showed a type A polymorph with predominant peaks appearing at $2\theta = 15.199^\circ$, 16.958° , 17.900° , and 22.941° . The RS4 nanoparticles subjected to homogenization did not show any peak, revealing that they were amorphous. Thus, these procedures seriously affected the repeat distance of crystalline and amorphous lamellae of starch granules. In sum, the amorphous state of the RS4 nanoparticles may play a more positive role in enhancing dissolution in vitro and internal adsorption compared with the crystalline state of RS4 in the study by Wang et al. (2011). Therefore, we conclude that homogenization is suitable for RS4 nanoparticle production.

RS4 nanosuspensions stability and swelling analysis

The swelling of the RS4 and RS4 nanoparticles are shown in Fig. 5A. The swelling of RS4 nanoparticle and RS4 was 13.01 and 2.24%, respectively. The swelling of RS4 nanoparticle was higher than those of RS4, which might be because of the formation of smaller-sized particles and melting of crystallites after high-speed shearing. Smaller particles provided higher surface area; hence increased the swelling.

As can be seen from Fig. 5B, when the storage time was increased 0 h to 24 h, no significant changes were obtained in the average size of RS4 nanosuspensions. This slight increase in the average size was caused by the ability of RS4 nanoparticles to imbibe moisture and expand

(swelling) while in water medium at 30 °C. Shi et al. (2011) also reported that some swelling of starch nanoparticles occurred when dispersed in water medium, which increased the mean particle size. In conclusion, the RS4 nanosuspensions showed good physical stability over the 24 h at 30 °C, indicating good shelf-life characteristic.

Conclusion

The present study demonstrated that homogenization combined with w/o miniemulsion cross-linking technique is a useful method to prepare and optimize RS4 nanoparticles. The application of a three-factor, three-level Box–Behnken experimental design combining RSM and quadratic programming was successful in reaching the global optimal solution for minimizing the z-average diameter of RS4 nanoparticles by high-pressure homogenization. DLS experiments revealed small size distribution of RS4 nanoparticles. XRD indicated that homogenization destroyed the crystalline structure of the RS4 nanoparticles. Stability analysis revealed that the particle size of RS4 nanosuspensions remained unchanged over 24 h at 30 °C. The prepared RS4 nanoparticles could be extensively used in biomedical applications and in the development of new medical materials.

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References

- Antonietti M, Landfester K (2002) Polyreactions in miniemulsions. *Prog Polym Sci* 27:689–757
- Asua JM (2002) Miniemulsion polymerization. *Prog Polym Sci* 27:1283–1346
- Chen W, Wang WP, Zhang HS, Huang Q (2012) Optimization of ultrasonic-assisted extraction of water-soluble polysaccharides from *Boletus edulis* mycelia using response surface methodology. *Carbohydr Polym* 87:614–619
- Chivrac F, Pollet E, Avérous L (2009) Progress in nano-biocomposites based on polysaccharides and nanoclays. *Mater Sci Eng R* 67:1–17
- Ding Y, Kan J (2016) Characterization of nanoscale retrograded starch prepared by a sonochemical method. *Starch-Starke* 68:264–273
- Ding Y, Zheng J, Xia X, Ren T, Kan J (2016a) Box–behnken design for the optimization of nanoscale retrograded starch formation by high-power ultrasonication. *Lwt-Food Sci Technol* 67:206–213
- Ding Y, Zheng J, Xia X, Ren T, Kan J (2016b) Preparation and characterization of resistant starch type IV nanoparticles through ultrasonication and miniemulsion cross-linking. *Carbohydr Polym* 141:151–159
- Ding Y, Zheng J, Zhang F, Kan J (2016c) Synthesis and characterization of retrograded starch nanoparticles through

- homogenization and miniemulsion cross-linking. *Carbohydr Polym* 151:656–665
- Espadabellido E, Ferreirogonzález M, Carrera C, Palma M, Barroso CG, Barbero GF (2016) Optimization of the ultrasound-assisted extraction of anthocyanins and total phenolic compounds in mulberry (*Morus nigra*) pulp. *Food Chem* 219:23–32
- Fuentes-Zaragoza E, Sánchez-Zapata E, Sendra E, Sayas E, Navarro C, Fernández-López J, Pérez-Alvarez JA (2011) Resistant starch as prebiotic: a review. *Starch-Starke* 63:406–415
- Hernandez M, Recio G, Martin-Palma RJ, Garcia-Ramos JV, Domingo C, Sevilla P (2012) Surface enhanced fluorescence of anti-tumoral drug emodin adsorbed on silver nanoparticles and loaded on porous silicon. *Nanoscale Res Lett* 7:364
- Lamprecht A, Ubrich N, Pérez MH, Lehr CM, Hoffman M, Maincent P (2000) Influences of process parameters on nanoparticle preparation performed by a double emulsion pressure homogenization technique. *Int J Pharm* 196:177–182
- Le Corre D, Bras J, Dufresne A (2010) Starch nanoparticles: a review. *Biomacromolecules* 11:1139–1153
- Liu R, Ma G, Meng FT, Su ZG (2005) Preparation of uniform-sized PLA microcapsules by combining Shirasu porous glass membrane emulsification technique and multiple emulsion-solvent evaporation method. *J Control Release* 103:31–43
- Mahmoudi Najafi SH, Baghaie M, Ashori A (2016) Preparation and characterization of acetylated starch nanoparticles as drug carrier: ciprofloxacin as a model. *Int J Biol Macromol* 87:48–54
- Niemann B, Sundmacher K (2010) Nanoparticle precipitation in microemulsions: population balance model and identification of bivariate droplet exchange kernel. *J Colloid Interface Sci* 342:361–371
- Pang SC, Chin SF, Tay SH, Tchong FM (2011) Starch–maleate–polyvinyl alcohol hydrogels with controllable swelling behaviors. *Carbohydr Polym* 84:424–429
- Patel CM, Chakraborty M, Murthy ZVP (2016) Fast and scalable preparation of starch nanoparticles by stirred media milling. *Adv Powder Technol* 27:1287–1294
- Prabhu S, Vaideki K, Anitha S (2017) Effect of microwave argon plasma on the glycosidic and hydrogen bonding system of cotton cellulose. *Carbohydr Polym* 156:34–44
- Shi AM, Li D, Wang LJ, Li BZ, Adhikari B (2011) Preparation of starch-based nanoparticles through high-pressure homogenization and miniemulsion cross-linking: influence of various process parameters on particle size and stability. *Carbohydr Polym* 83:1604–1610
- Swamy GJ, Muthukumarappan K (2016) Optimization of continuous and intermittent microwave extraction of pectin from banana peels. *Food Chem* 220:108–114
- Thys RC, Westfahl JH, Noreña CP, Marczak LD, Silveira NP, Cardoso MB (2008) Effect of the alkaline treatment on the ultrastructure of C-type starch granules. *Biomacromolecules* 9:1894–1901
- Wang F, Deng R, Wang J, Wang Q, Han Y, Zhu H, Liu X (2011) Tuning upconversion through energy migration in core–shell nanoparticles. *Nat Mater* 10:968–973
- Xu J, Sun J, Wang Y, Sheng J, Wang F, Sun M (2014) Application of iron magnetic nanoparticles in protein immobilization. *Molecules* 19:11465–11486