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Study on the Preparation Process of Poly (L-lactic acid)-icariin Drug-loaded Microspheres

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Abstract

The o/w type emulsification-solvent evaporation method was utilised to prepare the drug-carrying microspheres, with dichloromethane designated as the solvent phase, poly-L lactic acid as the carrier material, Icariin as the encapsulated drug, and Tween-80 as the emulsifier. The effects of ultrasonic time, ultrasonic power, volume ratio of internal and external phases, and dosage of poly-L lactic acid on the particle size, encapsulation rate, and drug loading rate of drug-carrying microspheres were explored during the preparation process of drug-carrying microspheres. The morphology of the drug-carrying microspheres was characterised by scanning electron microscopy, and the particle size and polydispersity index of the microspheres were characterised by nano-laser particle sizer. The optimal preparation of the drug-carrying microspheres was obtained as follows: The optimal parameters for the preparation of the drug-carrying microspheres were identified as follows: a Tween-80 concentration of 10 mg/mL, a poly(L-lactic acid) concentration of 25 mg/mL, an oil-to-water phase volume ratio of 1:2, an ultrasonic time of 15 min, and an ultrasonic power of 180 W.The drug-carrying microspheres of poly(L-lactic acid) were produced with a smaller particle size and better dispersion, and the encapsulation rate was 88.65%. The present study has the potential to furnish technical and parametric assistance for the fabrication of poly(L-lactic acid) drug-loaded slow-release microspheres.

Keywords

o/w emulsification-solvent evaporation method; poly(L-lactic acid); Icariin; drug-loaded microspheres; encapsulation rate; drug-loading rate.

1. INTRODUCTION

Poly L lactic acid (PLLA) has been extensively utilised in the domain of drug delivery systems, exhibiting notable advantages as a biodegradable polymer material, characterised by its exceptional biocompatibility [1], degradability properties, and the capability for controlled release[2]. In comparison with certain naturally degradable materials, such as collagen, PLLA has been shown to exhibit superior stability and processability. The molecular structure of PLLA can be meticulously tailored to yield materials with varying strengths and degradation rates, thus ensuring its suitability for a diverse range of applications[3]. Icariin (ICA), the primary bioactive constituent of the traditional Chinese medicine Epimedium, is categorised within the flavonoid glycoside class, exhibiting pharmacological properties that encompass anti-inflammatory, antioxidant, and antitumour activities[4]. However, the poor water solubility and low bioavailability of ICA limit its clinical application. The development of a microsphere delivery system for ICA is therefore of significant interest, as it has been shown to enhance stability, facilitate controlled release, and ensure targeted delivery of the drug.

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The preparation of drug-loaded microspheres is commonly achieved through emulsification-solvent volatilisation[5], with process parameters such as ultrasound time, ultrasound power, and oil-to-water-phase volume ratio exerting a substantial influence on microsphere morphology, particle size, and drug encapsulation rate. Furthermore, the selection of emulsifiers and polymeric surfactants has been demonstrated to play a pivotal role in the performance of microspheres. However, systematic studies on the preparation process of PLLA-ICA drug-loaded microspheres and their influencing factors are still relatively limited. The present study aims to investigate the effects of different factors on the performance of PLLA-ICA drug-carrying microspheres, and then optimise the preparation process to provide a theoretical basis for their application in drug delivery systems.

2. EXPERIMENTAL MATERIALS AND METHODS

2.1. Materials and Instruments

Experimental materials are shown in Figure 1:

Figure 1. The main experimental materials

Name of reagents	specification	companies
dimethyl sulfoxide (DMSO)	99%	Shandong Keyuan Biochemical Co.
Tween-80	Medicinal grade	Shanghai McLean Biochemical Technology Co.
Icariin(ICA)	98%	Xi'an Shennong Biotechnology Co.
dichloromethane	analytical purity	Tianjin Beichen Fangzheng Reagent Factory
polyvinyl alcohol(PVA)	Medicinal grade	Guangzhou Qihua Chemical Co.
Poly-L lactic acid	Medicinal grade	Jinan Daigang Biological Engineering Co.
deionised water	------	Experimental Centre of Stomatology, North China University of Science and Technology

The main instruments used in this thesis are shown in Figure 2:

Figure 2. The main experimental instruments

Instrument name	production company
Electronic Balance AR224CN	Shanghai Topsy Electronic Technology Co.
magnetic stirrer	Shanghai Jingxue Scientific Instrument Co.
Ultrasonic cell pulveriser	Shanghai Sheng Analytical Ultrasonic Instrument Co.
centrifuge	Hitachi Instruments, Japan
-80 degree refrigerator	Qingdao Haier Special Electric Appliances Co.
Vacuum Freeze Dryer	Beijing Sihuan Qihang Technology Co.
Laser particle sizer	Shanghai Yidian Physical & Optical Instrument Co.
ultraviolet spectrophotometer	Shanghai Spectrum Instrument Co.
Field Emission Scanning Electron Microscopy	Zeiss GEMINI450, Germany

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2.2. Preparation of microspheres

The PLLA-ICA drug-carrying microspheres were prepared by means of the O/W emulsification solvent volatilisation method. Initially, icariin was dissolved in a DMSO solution, and the solution was then mixed thoroughly to obtain the drug solution. Thereafter, the drug solution was added to dichloromethane dissolved in levulinic acid to obtain the oil phase. Tween80 was added to polyvinyl alcohol (PVA) and ultrasonically homogenised to obtain the aqueous phase. The oil phase was then added to the aqueous phase, and the mixture was sonicated to form an emulsion. The emulsion was then subjected to magnetic stirring at a rate of 400 r/min for a period of 12 hours, with the objective of facilitating the evaporation of the dichloromethane. Subsequent to this, the mixture was subjected to centrifugation at a speed of 15,000 r/min for a duration of 20 minutes, with the aim of achieving the separation and collection of microspheres. These microspheres were then subjected to a process of washing with distilled water, followed by pre-freezing in a refrigerator set at a temperature of -80°C for a period of 5 hours. Thereafter, the microsphere powder was obtained through the utilisation of a vacuum freeze dryer for a duration of 36 hours.

2.2.1 Effect of PLLA concentration on drug-loaded microspheres

In order to study the effect of PLLA concentration on PLLA-ICA drug-carrying microspheres, the drug-carrying microspheres were prepared according to the ultrasonic power of 180w, ultrasonic time of 15min, oil-water phase volume ratio of 1:2, Tween80 concentration of 10mg/mL, and PLLA concentration range of 5-45mg/ml.

2.2.2 Effect of utrasound time on drug-loaded microspheres

In order to study the effect of ultrasound time on PLLA-ICA drug-carrying microspheres, the drug-carrying microspheres were prepared according to the ultrasonic power of 180 w, the volume ratio of oil to water phase of 1:2, the concentration of PLLA of 25 mg/ml, the concentration of Tween80 of 10 mg/mL, and the range of ultrasonic time from 1 to 30 min.

2.2.3 Effect of ultrasonic power on drug-loaded microspheres

In order to study the effect of ultrasonic power on PLLA-ICA drug-carrying microspheres, the drug-carrying microspheres were prepared according to the ultrasonic time of 15 min, the volume ratio of oil to water phase of 1:2, the concentration of PLLA of 25 mg/ml, the concentration of Tween80 of 10 mg/mL, and the range of ultrasonic power of 90-360 w. The results were shown in the following table.

2.2.4 Effect of oil-water phase volume ratio on drug-loaded microspheres

In order to investigate the effect of oil-water phase volume ratio on PLLA-ICA drug-loaded microspheres, the drug-loaded microspheres were prepared according to the ultrasonic power of 180 w, ultrasonic time of 15 min, PLLA concentration of 25 mg/ml, Tween80 concentration of 10 mg/mL, and the range of the volume ratio of the oil phase to the water phase from 1:1 to 1:14.

2.2.5 Effect of Tween80 concentration on drug-loaded microspheres

In order to study the effect of Tween80 concentration on PLLA-ICA drug-carrying microspheres, the drug-carrying microspheres were prepared according to the ultrasonic power of 180w, ultrasonic time of 15min, oil-water phase volume ratio of 1:2, PLLA concentration of 25mg/ml, and the concentration range of Tween80 from 5 to 45mg/ml.

2.2.6 Characterisation of drug-loaded microspheres

A field emission scanning electron microscope (GEMINI450, Zeiss, Germany) was used to characterise the sample morphology. The samples were prepared under the following conditions: PLLA concentration of 25 mg/ml, ultrasonic power of 180 w, ultrasonic time of 15 min, oil-water phase volume ratio of 1:2, and Tween80 concentration of 10 mg/mL, and a

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Zetasizer Nano Laser Particle Sizing Analyser was used to determine the average particle size of the drug-carrying microspheres of PLLA-ICA, and the polydispersity index (PDI). The average particle size and polydispersity index (PDI) of PLLA-ICA were determined by Zetasizer Nano Laser Particle Size Analyser, and each sample was tested three times in parallel, and the standard deviation was calculated.

2.2.7 Determination of encapsulation rate and drug loading rate

The concentration of Icariin was determined by ultraviolet spectrophotometry. 10mg of microspheres were weighed precisely and added into 2ml of dichloromethane to fully dissolve the microspheres, and then 1ml of DMSO was added to make it mix well. Take an appropriate amount of this solution and add it to the sample cell, then measure the absorbance according to the absorption wavelength of the sample, so as to calculate the concentration of the sample.

Drawing of standard curve: accurately weigh the Epimedoside 4.0mg standard, add DMSO solution to the 20ml volumetric flask scale and shake well to dissolve until clarified. Then 0.3 mL, 0.6 mL, 0.9 mL, 1.2 mL, 1.5 mL, 1.8 mL, 2.1 mL, 2.4 mL of Epimedoside standard solution was sucked into a 20 mL volumetric flask, and DMSO was added to obtain the results of 3ug/ml, 6ug/ml, 9ug/ml, 12ug/ml, 15ug/ml, 18ug/ml, 21ug/ml, 24ug/ml, eight concentration points with a maximum absorption wavelength of 273nm, and the absorbance values were measured using DMSO solution as a blank control.

The equations for calculating the encapsulation rate and drug loading rate of the microspheres were as follows:

Encapsulation rate = (total mass of drug in microspheres/total mass of drug delivery) × 100%.

Drug loading rate = (mass of drug in microspheres / mass of microspheres) × 100%

3. RESULTS AND ANALYSES

3.1. Plotting of standard curve

As can be seen from Figure 3, when the concentration of Icariin ranges from 3-24ug/ml, the absorbance ranges from 0.071-0.764, there is an obvious linear correlation between the concentration of Icariin and the absorbance, and the linear equations fitted to accurately calculate the encapsulation rate of Icariin and the loading rate. The standard curve equation of Icariin:

$$Abs=0.03426C—0.03329$$

$$R^2 = 0.98823481$$

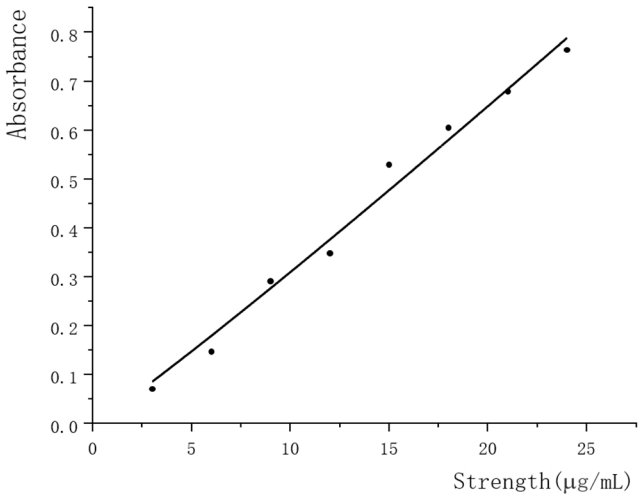


Figure 3. Standard curve of Icariin

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3.2. Determination of influencing factors

As can be seen from Figure 4, the effect of PLLA concentration on the encapsulation rate showed an increasing trend. At 5-16 mg/mL: the encapsulation rate was only 2.84%-6.23%, which was mainly due to the loose structure of microspheres caused by the insufficient concentration of PLLA, and the drug molecules were easy to leak through the pores. At 20-25 mg/mL, the encapsulation rate increased to 22.93%-35.05%, at which the polymer chains were entangled with each other to form a dense network, which effectively inhibited the release of drug[6]. At 30-45 mg/mL: the encapsulation rate fluctuated. This may be related to the increase in the viscosity of the polymer solution at high concentrations, resulting in uneven distribution of the drug during microsphere preparation. When the concentration of PLLA was in the process of gradual increase from 5 mg/mL to 45 mg/mL, the particle size of the nanomicrospheres showed a tendency to become smaller and then larger. This is because at lower PLLA concentrations, the microspheres will collapse internally during the curing stage, making it difficult to form a good spherical morphology[7]. As the PLLA concentration increases from 12 mg/mL to 45 mg/mL, the particle size of the nanomicrospheres gradually increases. This change was attributed to the increase in droplet breakage resistance due to the increase in solution viscosity at high polymer concentration, which resulted in less efficient dispersion to form emulsions and formation of larger particle sizes[8]. Considering all the performance parameters, the optimal PLLA concentration was 25 mg/mL: the average particle size of microspheres under this condition was 719.4 nm, the PDI was 0.482, and the encapsulation rate was 35.05%, and the preparation scheme was further optimised by exploring the effects of other conditions subsequently.

Figure 4. Effect of different PLLA concentrations on drug-loaded microspheres

Concentration of poly-L lactic acid (mg/ml)	Encapsulation rate	Drug loading rate	Average particle size(nm)	PDI
5	2.84%	0.20%	581.9±96.1	0.678±0.067
8	4.31%	0.16%	567.3±104.3	0.672±0.075
12	5.54%	0.17%	540.2±164.2	0.663±0.107
16	6.23%	0.17%	545.7±100.1	0.636±0.081
20	22.93%	0.30%	698.4±102.6	0.668±0.097
25	35.05%	0.33%	719.4±56.6	0.482±0.305
30	37.38%	0.29%	787.3±55.4	0.611±0.323
35	27.59%	0.22%	792.1±77.9	0.578±0.423
40	39.91%	0.30%	762.0±73.8	0.415±0.309
45	36.02%	0.21%	832.2±65.1	0.323±0.217

3.2.2 Effect of ultrasound time on drug-loaded microspheres

As shown in Figure 5, the effect of ultrasound duration on the encapsulation rate of microspheres showed a parabolic trend of increasing and then decreasing with the prolongation of the ultrasound time: the encapsulation rate gradually increased from 76.63%

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to the peak value of 88.65% in the interval of 1-15 minutes, and then further decreased to 84.47% at 30 minutes. The change of drug loading rate was basically synchronous with the encapsulation rate, reaching a peak value of 0.51% at 15 min, and then decreased. The mechanism of this phenomenon can be divided into two phases: the positive effect phase (1-15 min): the shear force generated by the ultrasonic cavitation effect effectively enhances the mass transfer efficiency at the oil-water phase interface[9], which promotes the diffusion of drug molecules into the interior of the microspheres, and improves the encapsulation efficiency by about 12%. Negative effect stage (15-30 min): too long ultrasound may cause three unfavourable effects: (1) the local high temperature generated by the rupture of cavitation bubbles leads to the degradation of drug molecules; (2) mechanical shear destroys the structure of the microspheres [10], which triggers the leakage of the drug; (3) the excessive depletion of surfactant leads to the decrease of the interfacial stability. Particle size distribution parameters show that the average particle size decreases and then increases with the extension of ultrasound time: the particle size tends to decrease when the ultrasound time is 1-20 min, and reaches a minimum value of 410.7 nm at 20 min, and the particle size gradually increases beyond 20 min, and then increases to 623.7 nm at 30 min. This change is due to the dynamic regulation of the ultrasound energy on the process of droplet fragmentation and agglomeration[10], in the initial stage (1-20 min): the cavitation effect is caused by the high temperature and the high temperature of the droplet. In the initial stage (1-20 min), the cavitation effect dominates and the shear force continues to break up the droplets; in the transition stage (20-30 min), the agglomeration effect exceeds the fragmentation effect and the collision frequency between the particles increases, and the PDI value reaches a minimum of 0.123 at 25 min, which shows the optimal particle homogeneity. This phenomenon is closely related to the distribution of cavitation energy: moderate ultrasound (15-20 min) results in a uniform distribution of energy, whereas prolonged ultrasound results in an uneven energy density[11], which in turn increases the particle size dispersion. The combination of encapsulation efficiency (>80%), drug loading capacity (>0.5%) and particle size uniformity (PDI<0.18) showed that 15 min ultrasound was the optimal process parameter. The average particle size of the microspheres prepared under these conditions was 499.7 nm, and the PDI value was 0.176, which showed good drug loading capacity and stability.

Figure 5. Effect of different ultrasound time on drug-loaded microspheres

ultrasound time (min)	Encapsulation rate	Drug loading rate	Average particle size(nm)	PDI
1	76.63%	0.39%	775.3±78.4	0.582±0.397
3	74.92%	0.4%	817.3±48.3	0.342±0.291
5	82.76%	0.42%	582.6±31.2	0.205±0.086
10	82.75%	0.44%	536.6±7.1	0.172±0.085
15	88.65%	0.51%	499.7±13.1	0.176±0.063
20	85.02%	0.39%	410.7±4.9	0.200±0.036
25	83.23%	0.42%	537.3±4.1	0.123±0.072
30	84.47%	0.45%	623.7±4.3	0.135±0.068

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3.2.3 Effect of ultrasonic power on drug-loaded microspheres

From Figure 6, it can be seen that the influence of ultrasonic power on the formation process of microspheres shows the energy threshold effect. When the ultrasonic power was in the range of 90-120 W, the oil-water phase could not form a stable emulsion structure because the energy threshold was not breached, resulting in the failure of microsphere formation. This phenomenon illustrates the critical role of ultrasonic energy in the microsphere forming stage. When the power was increased from 180W to 360W, the encapsulation rate decreased from 79.62% to 51.74%, and the drug loading rate decreased from 0.45% to 0.33%. This phenomenon is presumed to be due to the synergistic effect of drug leakage caused by the destruction of microsphere structure due to mechanical stress and degradation of drug molecules caused by local thermal effect[10]. The change of particle size showed a two-stage pattern: in the region of 180-270 W, the particle size was stable at about 580 nm, showing a dynamic balance between fragmentation and agglomeration; when the power was 360 W, the particle size increased to 714.5 nm, which can be attributed to the increase of particle collision frequency due to the enhancement of cavitation effect, which led to the enhancement of the agglomeration process[11]. Comprehensive analysis showed that ultrasonic power affects the energy transfer efficiency by modulating the intensity of cavitation effect, which in turn determines the structural integrity and drug loading capacity of microspheres. A comprehensive evaluation showed that 180 W was the optimal ultrasonic power for the preparation of microspheres. The average particle size was 582.8 nm, the encapsulation rate was 79.62%, and the drug loading rate was 0.45%, which were significantly higher than the other power groups. Compared with other power conditions, the 180W ultrasonic treatment ensured the efficient loading of the drug while effectively controlling the particle size and dispersion of the microspheres.

Figure 1. Effect of different ultrasonic power on drug-loaded microspheres

ultrasonic power (W)	Encapsulation rate	Drug loading rate	Average particle size(nm)	PDI
90	No microspheres	——	——	——
120	No microspheres	——	——	——
180	79.62%	0.45%	582.8±34.3	0.537±0.324
270	61.51%	0.35%	584.1±25.0	0.364±0.188
360	51.74%	0.33%	714.5±42.8	0.521±0.374

3.2.4 Effect of oil-water phase volume ratio on drug-loaded microspheres

Figure 7 shows that there is a negative correlation between the encapsulation rate of microspheres and the volume ratio of oil and water phases. When the oil-water ratio decreases from 1:1 to 1:14, the encapsulation rate decreases from 86.71% to 6.94%. This is due to the change of oil-water interfacial area: when the oil phase is a continuous phase (e.g., oil-water ratio of 1:1), it can provide a larger interfacial adsorption area, which promotes the effective encapsulation of the drug molecules; when the ratio of the aqueous phase is increased (e.g., oil-water ratio of 1:14), the oil phase can not encapsulate the drug efficiently, which results in drug molecules diffusing to the outer aqueous phase more easily. The average particle size shows a trend of decreasing and then increasing, the oil phase continuous phase: the formation of 680.6nm larger particles; the best emulsification phase: the particle size down to 467.1nm; the water phase continuous phase: the particle size increased to 843.1nm.This change is due to the

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change of the interfacial tension: the oil-water ratio of 1:1.5, the PDI is the lowest value of 0.202, the interfacial tension reaches a minimum, this change is conducive to the improvement of the drug molecules; the oil-water ratio of 1:1.5, PDI is the lowest value 0.202, the interfacial tension reached a minimum, and the interfacial tension decreased. The decrease of interfacial tension is conducive to improve the stability of the emulsion[12], at this time, the particle size distribution is the most uniform; while the oil-water ratio of 1:14, the interfacial tension increases, the oil phase is not sufficiently dispersed to lead to the agglomeration of the particles, and the PDI is as high as 0.559. Taking into account the encapsulation rate (>60%), the drug loading rate (>0.35%), and the distribution of the particle size (PDI <0.3), the oil-water ratio of 1:2 is the optimal process parameter. The best process parameters were found to be 1:2 oil/water ratio. Under this condition, the encapsulation rate was 63.54%, the loading rate was 0.31%, the average particle size was 591.4 nm, and the PDI was 0.273.

Figure 2. Effect of different oil-water phase volume ratios on drug-loaded microspheres

Oil-water phasevolume ratio	Encapsulation rate	Drug loading rate	Average particle size(nm)	PDI
1:1	86.71%	0.38%	680.6±31.3	0.311±0.134
1:1.5	53.21%	0.33%	467.1±14.2	0.202±0.121
1:2	63.54%	0.31%	591.4±29.9	0.273±0.037
1:5	44.70%	0.38%	683.1±37.5	0.456±0.142
1:8	20.60%	0.39%	845.9±98.2	0.552±0.049
1:11	19.73%	0.47%	764.1±41.6	0.518±0.034
1:14	6.94%	0.44%	843.1±75.9	0.559±0.063

3.2.5 Effect of emulsifiers and polymeric surfactants on drug-carrying microspheres

Polyvinyl alcohol (PVA) is an efficient emulsifier and stabiliser due to its excellent amphiphilicity and its ability to enhance the aqueous phase viscosity and adsorb at the water-oil interface[13]. However, although the use of PVA as an emulsifier was able to prepare microspheres with smooth surfaces, there was obvious adhesion between the microspheres and poor dispersion as seen in Figure 8. In order to solve this problem, we introduced the nonionic surfactant Tween80 as a co-emulsifier in the system. Figure 9 shows the SEM images of microspheres prepared with Tween80 and PVA as co-emulsifiers. As can be seen from the figure, the dispersion of the microspheres was significantly improved and the adhesion was drastically reduced. This is mainly attributed to the fact that Tween80 not only possesses the emulsifying function, but also the dispersing function[14].The molecular structure of Tween80 consists of hydrophobic fatty acid chains and hydrophilic polyoxymethylene chains, which is a unique structure that enables the formation of stable micellar structure between the aqueous phase and the oil phase[15], which enhances the interfacial viscosity and promotes the homogeneous distribution of dispersed phases in the continuous phase. In addition, Tween80 can effectively reduce the surface tension of the liquid, inhibit the aggregation and condensation of droplets, and further improve the stability of the system.

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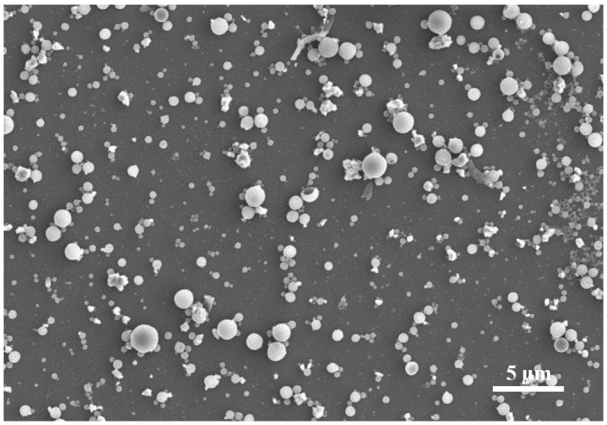


Figure 8. Microspheres prepared with Tween80

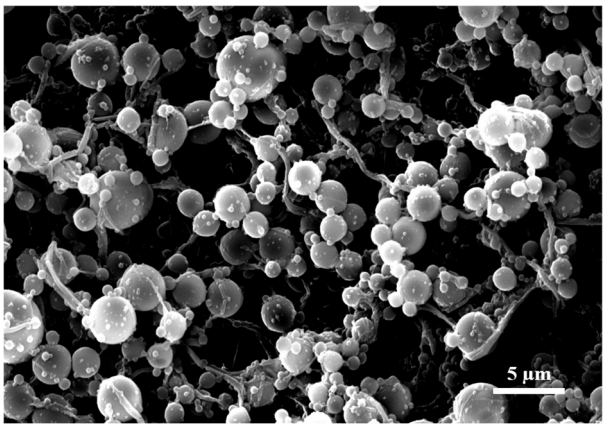


Figure 9. Microspheres prepared without Tween80

The amount of emulsifier has a significant effect on the microsphere surface state and particle size distribution. By adjusting the amount of emulsifier, the desired particle size range can be obtained while ensuring the morphology of microspheres. As shown in Figure 10, as the concentration of Tween 80 in the aqueous phase was gradually increased from 1 mg/mL to 30 mg/mL, the average particle size of the microspheres showed a tendency to decrease, and its particle size distribution index (PDI) was maintained at a low level. This phenomenon was attributed to the decrease of surface tension of the aqueous phase due to the increase of surfactant concentration, which enhanced the dispersive force of the oil phase in the aqueous phase and formed a hydrophilic film between the two, which effectively inhibited aggregation among the microspheres and enhanced the stability of the system[15]. However, when the surfactant concentration exceeded 30 mg/mL, the particle size and PDI of the microspheres increased, which could be attributed to the fact that the high concentration of surfactant induced the formation of stick or multilayer structures, which negatively affected the formability of microspheres[16]. On the other hand, the concentration of Tween 80 in the range of 1-10 mg/mL promoted the encapsulation efficiency from 30.8% to 67.1% due to the increase in viscosity of the aqueous phase, which reduced the diffusion rate from the oil phase to the aqueous phase. However, when the concentration of Tween 80 was further increased, its encapsulation efficiency decreased instead, which was speculated to be possibly due to the emulsion droplet size being too small to form a sufficiently thick and dense protective film[17], resulting in more drug loss into the aqueous phase. Based on the combined consideration of microsphere particle size and encapsulation rate, the optimal concentration of Tween 80 in the aqueous phase was 10 mg/mL.

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Figure 3. Effect of different Tween80 concentration on drug-loaded microspheres

Tween80 concentration (mg/ml)	Encapsulation rate	Drug loading rate	Average particle size(nm)	PDI
1	30.8%	0.17%	791.4±10.49	0.192±0.085
5	28.1%	0.15%	765.3±27.78	0.324±0.101
10	67.1%	0.32%	660.5±21.1	0.224±0.06
20	50.5%	0.37%	553.3±28.9	0.267±0.05
30	49.8%	0.33%	527.3±47.5	0.306±0.103
40	55.6%	0.33%	632.1±44.5	0.243±0.08
50	38.3%	0.35%	710.4±22.2	0.264±0.05

4. SUMMARY

In this study, PLLA-ICA drug-carrying microspheres were prepared by emulsification-solvent evaporation method, and the effects of ultrasound time, ultrasound power, oil-water phase volume ratio, PLLA concentration, and Tween80 concentration on the morphology of the microspheres, the particle size, and the drug-carrying rate of the drug encapsulation were systematically investigated. The experimental results showed that the PLLA-ICA drug-loaded microspheres prepared with Tween-80 concentration of 10 mg/mL, PLLA concentration of 25 mg/mL, oil-water phase volume ratio of 1:2, ultrasonic time of 15 min, and ultrasonic power of 180 W had a good morphology and high encapsulation rate. This study provides a basis for process optimisation for the preparation of PLLA-ICA drug-carrying microspheres, which lays the foundation for their application in drug delivery systems. Future studies can further explore the drug release behaviour of microspheres and their pharmacodynamic performance in vivo to promote their application in the clinic.

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