THE EFFECT OF PROCESSING PARAMETERS ON CHARACTERISTICS OF PLLA MICROSPHERES

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Introduction

Biodegradable micro- and nanospheres made of poly-l-lactide (PLLA) are very potent drug or antigen delivery systems with inherent potential for drug and antigen targeting. Control of sphere size and size distribution are the ultimate goals of drug delivery. A particular release rate and desired route of administration typically require a particular sphere size. The objective of this study is to formulate modified PLLA microparticles with defined size and shape that can efficiently bind bioactive component. This study investigates the effects of some process variables on the size distribution of particles prepared by precipitation method [1,2]. The main focus is to study the effect of co-solvent selection and PVA concentration on the shape, size and X-ray diffraction (XRD) of the particles [3,4].

Materials and Methods

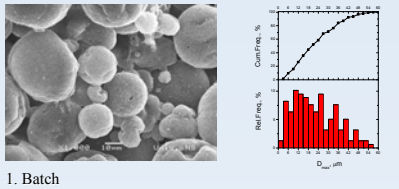
Poly-l-lactide with an average molecular weights of 100 000 g/mol was purchased from Sigma Company (SIGMA-Aldrich, Germany). PVA was used as stabilizing agent. Chlorophorm, methanol, ethanol and other reagents were LC grade and used as received.

Briefly, the method was performed as follows: 50 mg of commercial granules PLLA (SIGMA-Aldrich, Germany) were dissolved in chlorophorm, and this solution was added to methanol or ethanol to form a dispersion. This dispersion was added dropwise to 20 ml PVA solution containing 0.5-1 wt% of PVA while the mixture was stirred at 1200rpm using magnetic stirrer. After that solution was centrifuged 2 hours on 4000 rpm, decanted and dried overnight. Scanning electron microscopy (SEM), Stereological analysis and X-ray diffraction (XRD) are used to characterize the particles.

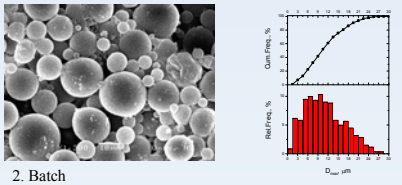
Variables

Batch	Co-solvent	PVA, w/v
1.	MeOH	0.5%
2.	MeOH	1%
3.	EtOH	0.5%
4.	EtOH	1%

Results and discussion



1. Batch



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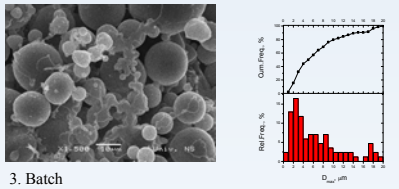

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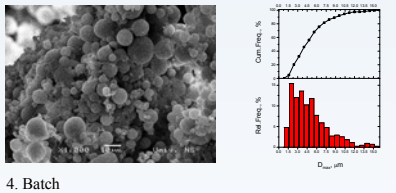

4. Batch

Fig. 1. SEM images of PLLA microspheres

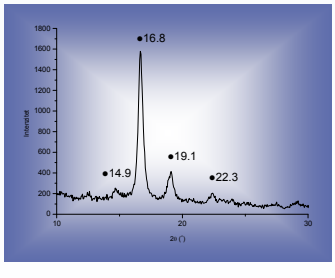

Fig. 2. XRD pattern of products prepared by addition of PLLA into PVA solution

Characterization of particle morphology and size

The surface morphology and size of microparticles were studied by scanning electron microscopy (SEM). A bit of PLLA powder was deposited on a metal plate and sputtered for few minutes with gold and, finally, analyzed with SEM (JEOL JSM-6460LV). The particle size and morphology were examined by semi-automatic image analyzer (Videoplan, Kontron), connected with scanning electron microscope (SEM).

From SEM recordings we can see that all particles are spherical. In the first and the second series, the particles are large with a large size distribution. In the third and the fourth series particles are smaller and more uniform.

From the results obtained from the stereological examine we can see that particles from the first and the second series are larger with mean diameter 22.38 and 10.94 μm, respectively. In the third and the fourth series particles are smaller and more uniform. Mean diameter of the particles is 6.69 and 4.93 μm, respectively.

XRD examination

X-ray diffraction patterns were measured using X-ray powder diffractometer (Bruker D8 Advance) The XRD experiments were performed in symmetrical reflection mode with Cu Kα radiation (1.54 Å) using Göbel Mirror bent gradient multilayer optics. The angular range was from 10° to 30° with the steps of 0.05° and the measuring time was 6 s per step.

Fig. 2 shows the XRD pattern of the products prepared using PVA solution. The pattern exhibits significant peaks at 2θ=14.9, 16.8, 19.1 and 22.3° in agreement with the peaks at 15, 16, 18.5 and 22.5 for a PLA homopolymer.

Conclusion

By the selection of the co-solvent in the inner phase, one may dramatically alter the properties of PLLA microparticles prepared by a modified precipitation method. Optimal particles are achieved with ethanol and higher PVA concentration.

References

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