VARIABLES ON SIZE DISTRIBUTION

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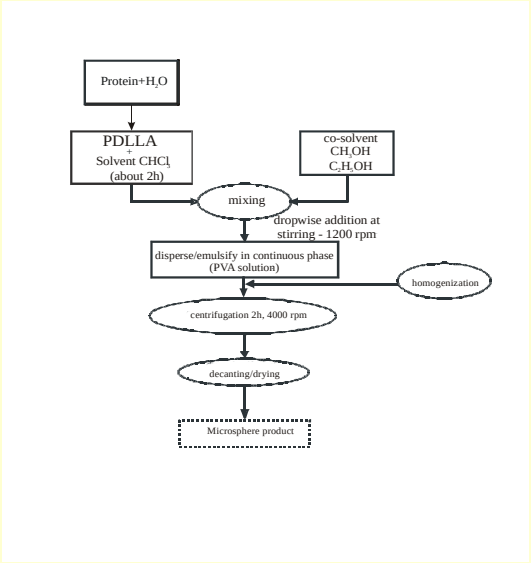
Abstract

Worldwide, there is u currently considerable care for the development of biodegradable microspheres as systems for controlled release of medicaments. The major disadvantage of traditional administration routes of medicaments is the need for frequent repetition. Encapsulation has been proven to be an effective vehicle for the controlled delivery of various medicaments. The encapsulation efficiency and release kinetics of the medicaments have been found to be dependent upon the size of the microspheres synthesized. The aim of this study was to formulate microparticles from poly-dl-lactide (PDLLA) by modified precipitation method. Bovine serum albumin (BSA) was used as a model protein for encapsulation. The surfactant polyvinyl alcohol (PVA) was incorporated to increase encapsulation efficiency and to achieve PDLLA spheres with desired size. The main focus was to study the effect of co-solvent selection (methanol or ethanol), PVA concentration, chloroform-to-water ratio, the speed and time of homogenization and solvent removal rate on the properties of microparticles. The average size and morphology of microparticles varied substantially among these preparation conditions. An increase in stirring rate and time of homogenization and concentration of stabilizer agent were found to reduce moderately the size of microparticles. Other process parameters had limited influence on particle size.

Introduction

A number of different polymers, both synthetic and natural, have been utilized in formulating biodegradable nanoparticles. Polylactides (PLA) and poly (D,L-lactide-co-glycolide) (DLPLGA) have been extensively investigated for drug delivery [1-4]. As polyesters in nature, these polymers undergo hydrolysis upon implantation into the body, forming biologically compatible and metabolizable moieties (lactic acid and glycolic acid) that are removed from the body by the citric acid cycle. Polymer biodegradation products are generated at very slow rate, thus not affecting normal cell function.

Methods



Conclusion

Experiments presented in this work were designed to investigate the effect of various process parameters on the properties of PDLLA microspheres obtained by modified precipitation method. The main advantage of this method is that it does not require an increase of temperature and, therefore, may be useful when heat sensitive drugs are used for encapsulation. In order to synthesize small microspheres, the date indicates that is ideal to have a high PVA concentration, a low chloroform to water ratio, and high homogenization speed.

Results

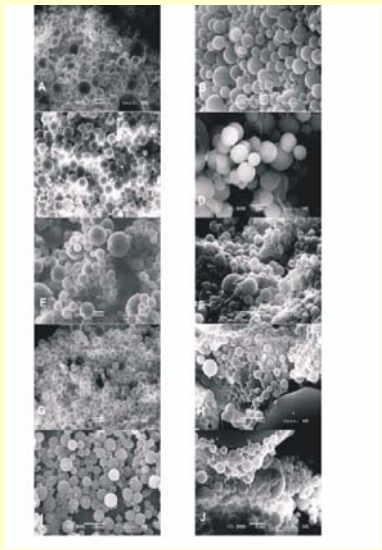


Fig. 1. SEM images of PDLLA microspheres prepared by precipitation method. The size of the bar is 10 μm in A ,C, E, G and I and 5 μm in B,D, F, H and J. All batches are numbered as listed in Table 1.

Batch No.	Co-solvent	Chloroform (ml)	Co-solvent, (ml)	PVA (1.0%), (ml)	Homogenizer speed (rpm)	Chloroform to water ratio
A.	EtOH	1.5	3	30	1 min, 10 000	1:20
B.	EtOH	1.5	3	30	1 min, 21 000	1:20
C.	EtOH	1.5	3	20	10 min, 10 000	1:13.33
D.	EtOH	1.5	3	20	10 min, 21 000	1:13.33
E.	MeOH	1.5	3	20	1 min, 10 000	1:13.33
F.	MeOH	1.5	3	20	1 min, 21 000	1:13.33
G.	MeOH	1.5	2.5	20	10 min, 10 000	1:13.33
H.	MeOH	1.5	2.5	20	10 min, 21 000	1:13.33
I.	MeOH	6x1.5	6x3.5	20	-	1:2.22
J.	MeOH	6x1.5	6x3.5	20*	-	1:2.22

*(5.0%) PVA

Table 1. The preparation conditions for precipitation method for obtaining PDLLA microspheres

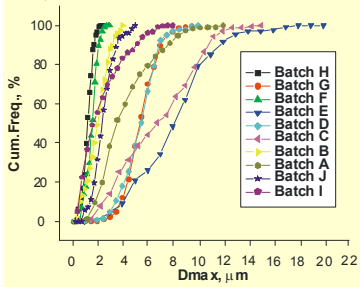


Fig. 2. Size distribution of microspheres of the 10 batches over Dmax prepared by precipitation method. All batches are numbered as listed in Table 1.

From the SEM images we can se that all particles are spherical with smooth surface. The average diameter of the microparticles prepared by precipitation method is smaller with methanol (Fig. 1. E-J) then ethanol (Fig. 1. A-D). This observation was attributed to the higher water solubility of methanol, which caused that microparticles are formed faster. The smallest spherical particles are obtained in Batch H (Fig , 1) with methanol as co-solvent and 10 min of homogenization on 21 000 rpm.

Table 2. Influence of co-solvent and PVA concentration on the size of BSA-loaded microspheres

Batch No.	Co-solvent	PVA
A.	EtOH	30 ml, 1%
B.	EtOH	20 ml, 5%
C.	MeOH	20 ml, 5%
D.	EtOH	30 ml 1% +4 mg BSA

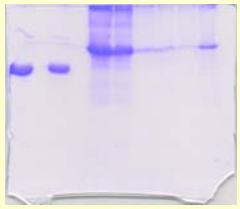


Fig 4. The SDS-PAGE analysis of BSA-loaded microspheres

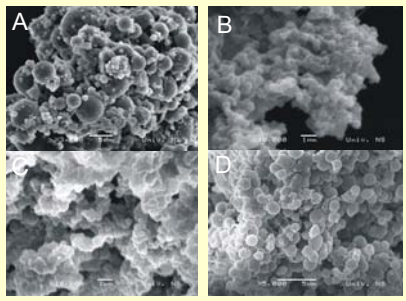


Fig. 3. SEM images of BSA-loaded PDLLA microspheres prepared by precipitation method. The size of the bar is 5 μm. All batches are numbered as listed in Table 2.

Table 3. Influence of solvent, co-solvent and PVA concentration on the size of HRP-loaded microspheres

Batch No.	Solvent	Co-solvent	PVA
E.	Chloroform	EtOH	30 ml, 1%
F.	Toluol	EtOH	30 ml, 1%
G.	Chloroform	MeOH	20 ml, 5%
H.	Chloroform	EtOH	20 ml, 5%

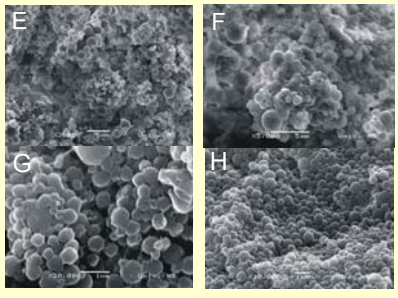


Fig. 5. SEM images of HRP-loaded PDLLA microspheres prepared by precipitation method. The size of the bar is 5 μm. All batches are numbered as listed in Table 4.

References

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