Comparative Study of Biodegradable Polymers on the Particle Size, Surface Morphology and Encapsulation Efficiency of Ketoprofen Loaded Nanoparticles

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Introduction

Drug loaded polymer nanoparticles

+ Ensure a number of advantages compared to free drug:
- ✓improving the selectivity and efficiency of the drug
- ✓increase of bioavailability in the case of poorly water-soluble drug
- ✓protection of drug from inactivation in the GIT
- ✓protection of mucosa from the toxicity of drug
- ✓increase of therapeutic index due to the reduction of the systemic absorption and/or side effect of the drugs
- ✓controlled drug delivery, delayed and/or prolonged drug action in the application site

Poly D,L lactic acid (PDLLA) Poly-ε-caprolactone (PCL)

+Widely used biocompatible and biodegradable hydrofobic polymers

+Approved by WHO and possesses the Generally Regarded as Safe (GRAS) status of the FDA as carriers for controlled delivery of different active pharmaceutical ingredients

Ketoprofen (KET)

+Non-Steroidal Anti-Inflammatory Drug (NSAID)

+Exhibits anti-inflammatory, analgesic, and antipyretic effects by acting as an inhibitor of the body's production of prostaglandins

-Cause GIT disorders including irritation, bleeding and ulceration

-Frequency of drug administration

Aims

✓Develop the polymeric nanocarriers for ketoprofen delivery

✓Investigate the influence of the polymer type on important properties of ketoprofen loaded biodegradable nanoparticles, such as particle size, roundness, smoothness, formation of aggregates and encapsulation efficiency

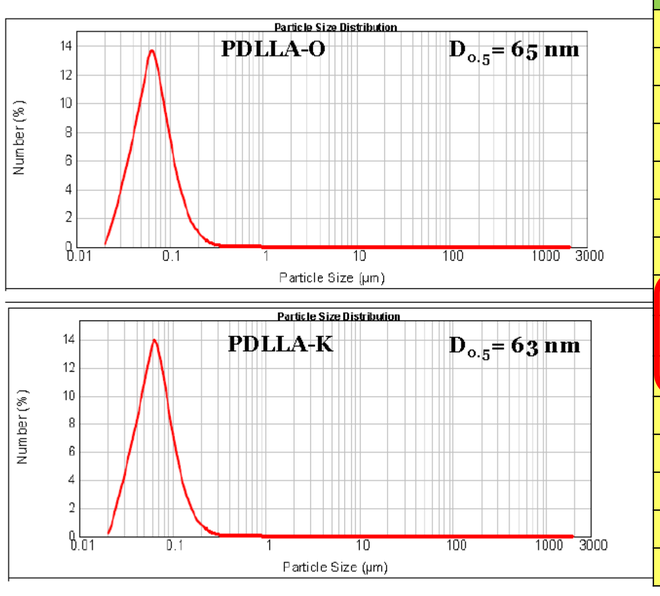
Metodology

KET loaded PDLLA/PCL nanoparticles were obtained by modified precipitation method : the commercial PDLLA/PCL granules and KET were dissolved in chloroform; this solution was first added drop-wise to ethanol and then into an aqueous solution containing PVA; the resultant dispersion was stirred at high speed (21 000 rpm) and centrifuged for 1 h on 4000 rpm; after the supernatant liquid was removed, the nanoparticles were dried at room temperature.

In order to characterize the obtained dry powder samples, folowing methods were employed:

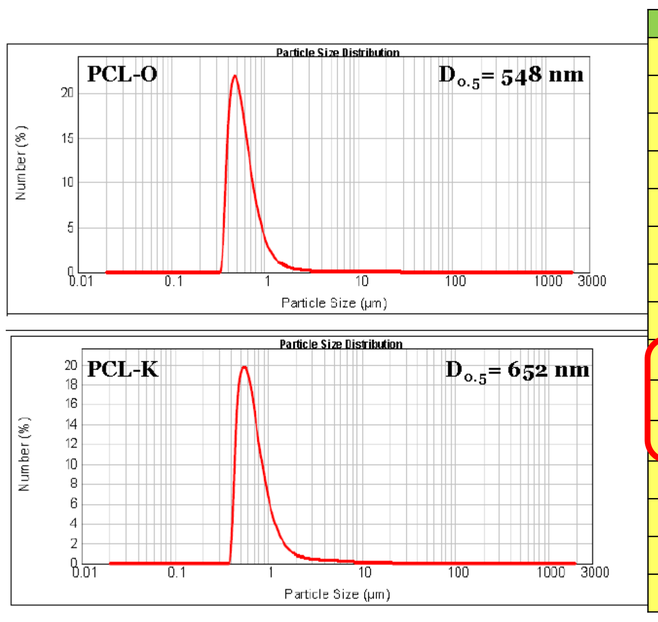
- ✓laser light diffraction
- ✓field emmision scanning electron microscopy
- ✓drug loading efficiency

Results



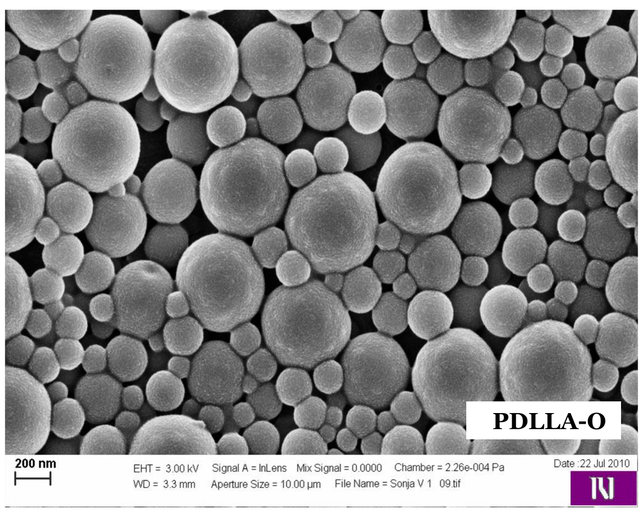
Size (µm)	Number in %
0,020	0,53
0,023	1,82
0,026	3,20
0,030	4,68
0,035	6,22
0,040	7,88
0,046	9,61
0,052	**11,44**
0,060	**12,61**
0,069	**11,28**
0,079	9,25
0,091	7,06
0,105	5,12
0,120	3,54
0,138	2,34

Figure 1.Particle size distribution pattern of drug free (PDLLA-O) and drug loaded PDLLA nanoparticles (PDLLA-K)



Size (µm)	Number in %
0,182	0,00
0,209	0,00
0,240	0,00
0,275	0,00
0,316	0,00
0,363	0,00
0,417	0,06
0,479	10,93
0,550	**17,46**
0,631	**17,62**
0,724	**15,31**
0,832	11,63
0,955	8,55
1,096	5,78
1,259	3,86

Figure 2. Particle size distribution pattern of drug free (PCL-O) and drug loaded PDLLA nanoparticles (PCL-K)



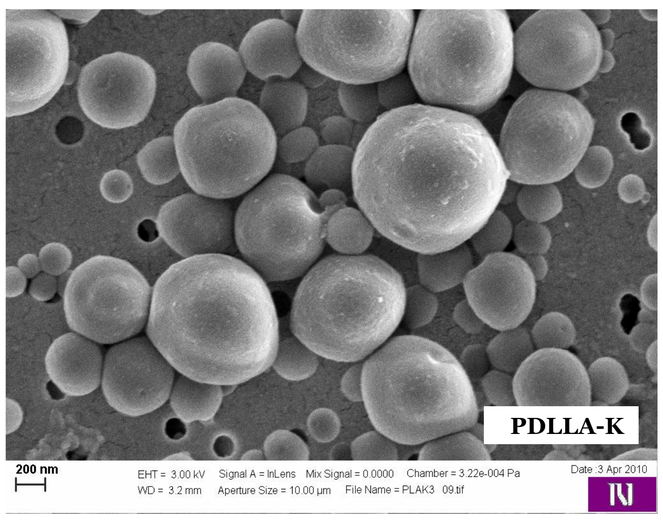
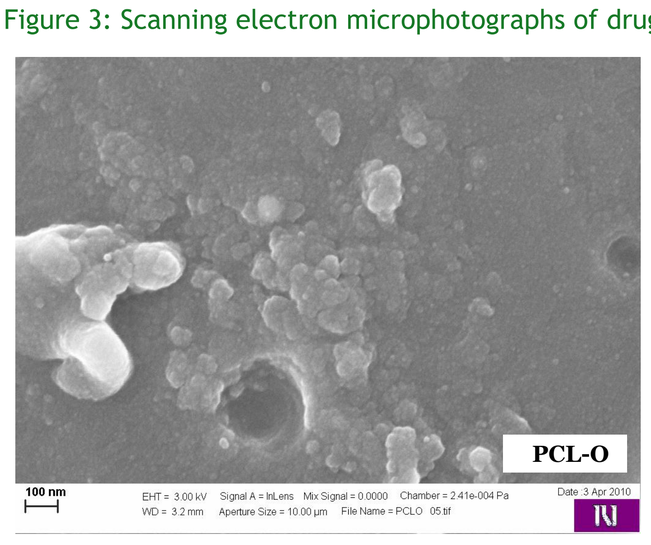


Figure 3: Scanning electron microphotographs of drug free (PDLLA-O) and drug loaded PDLLA nanoparticles (PDLLA-K)



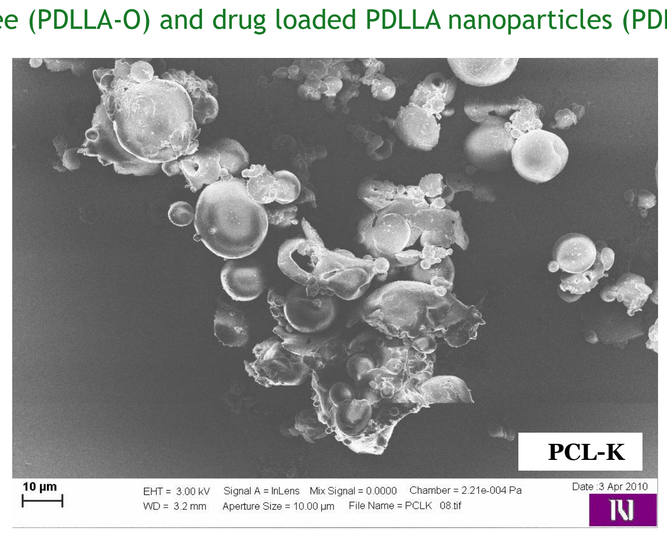


Figure 4: Scanning electron microphotographs of drug free (PCL-O) and drug loaded PCL nanoparticles (PCL-K)

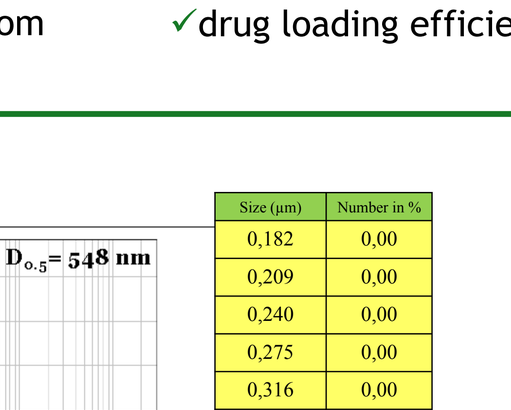


Figure 7. Chromatogram of the ketoprofen in a sample solution

Figure 5: HPLC patterns of ketoprofen loaded PDLLA nanoparticles

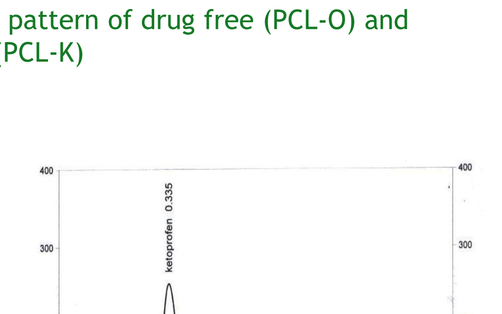


Figure 6: HPLC patterns of ketoprofen loaded PCL nanoparticles

Conclusions

- ➢ The resulting nanoparticles are dramatically different.
- ➢ Modified precipitation method used in this work is suitable only for preparing ketoprofen loaded PDLLA nanoparticles.
- ➢ Since the results for PCL particles showed low encapsulation efficiency, sub-micron particle size and agglomeration, the used method is unadapted and has to be adjusted by changing the variable parameters in formulation, such as the type and concentration of the stabilization factor, and organic-aqueous volume phase ratio.

Disscusion

➢Fig.1 illustrates narrow particle size distribution of the PDLLA nanoparticles; 50% of the nanoparticles present in drug free PDLLA nanoparticles and drug loaded PDDLA nanoparticles are smaller than 65 nm and 63 nm, respectively.

➢Size analyses of the ketoprofen free and ketoprofen loaded PCL nanoparticulate systems also show narrow particle size distribution but average diameters are about 600 nm (Fig.2).

➢Drug encapsulation doesn't cause any changings of shape and surface characteristics of PDLLA nanoparticles; all particles have a perfectly spherical shape with smooth surfaces and no agglomeration present (Fig.3).

➢However, PCL formulations show particle agglomeration and no spherical shape (Fig.4).

➢The results obtained by HPLC show a significant difference between the analysed samples; PDLLA nanoparticles of ketoprofen were obtained with encapsulation efficiency of 75% (Fig.5), while the drug loading efficiency in PCL nanoparticulate system was only 22 % (Fig.6).

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