

Control of particle size and drug release of PLA/PLGA microspheres

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Poly (D,L-lactic-co-glycolic acid) (PLGA) and poly (lactic acid) (PLA) are well known by its biocompatibility and biodegradability in biomedical solutions [1]. The PLGA/PLA microspheres are one of the most successful drug delivery systems (DDS) in lab and clinic [2]. In the present study, microspheres based on blend of PLGA and PLA with ibuprofen as drug and with poly(vinyl alcohol) as emulsifier were prepared by a developed double emulsion oil-in-water-in-water solvent evaporation method and characterized. The blend of PLA and PLGA is formed only by physical interactions between them. This can be seen from the FTIR spectrum which shows both PLA and PLGA component (Figure 1). The effect of added surfactant, PVA [poly (vinyl alcohol)] and PLA/PLGA concentration and emulsion speed stirring on the size of the resultant PLGA/PLA microspheres has been studied. Ibuprofen release profile from PLGA/PLA microspheres with PVA as emulsifier within a phosphate buffer solutions (PBS) is determined and compared to drug release profile of microspheres with different concentrations of PLGA and PLA. This experiment involves the use of PBS as the release medium to regulate the drug release. It was prepared using 0,2 M monobasic and 0,2 M dibasic sodium phosphate to achieve pH 7.4 at 37 °C [3]. A centrifugation process followed by a drying process at 40 °C during 4 h was carried out to obtain microspheres ready for drug release experiments. The PLA/PLGA microspheres were characterized by Zeta-sizer Nano ZS to assess their size. FT-IR analysis was used to assess the functional groups present in the PLA/PLGA microspheres. SEM was used to observe the shape and to corroborate the microspheres formation. Thermogravimetric analysis (TGA) was performed from 30 to 700 °C under nitrogen atmosphere on ibuprofen, PLA/PLGA microspheres-Ibuprofen, PLA/PLGA microspheres-Ibuprofen after the drug release experiment in PBS media and PLA/PLGA without ibuprofen. It was found that the particle size of microspheres could be easily controlled by varying the different parameters ([PVA], [PLA/PLGA] and emulsion speed stirring). It was also proved that drug release could be controlled by varying the particle size. Figure 2 shows the variability of the size distribution with different emulsion speeds (12.000 and 16.000 rpm). Likewise, the comparison of the size distribution by

varying the PVA and PLA/PLGA concentration were studied. The overall results of this study showed that the formula using 25 wt.% PLA and 75 wt.% PLGA, 1% w/v of PVA and 12.000 rpm of stirring speed produced the microspheres with the most uniform size distribution of 450-550 nm. Figure 3 shows PLA/PLGA-Ibuprofen drug release profiles determined by UV-Vis spectroscopy. Three types of microspheres were prepared for this study by the same method but with different concentrations of PLA and PLGA. Results indicate that if the size distribution is controlled, better release profiles are obtained. The microspheres with the most uniform size distribution (25 wt.% PLA and 75 wt.% PLGA, 1% w/v of PVA and 12.000 rpm of stirring speed) exhibit lower release rate achieving its full release at about 60 min. Instead, the drug release profile of 50 wt.% PLA and 50 wt.% PLGA microspheres and 75 wt.% PLA and 25 wt.% PLGA microspheres, which have a worse size distribution, achieve its full release at about 10 and 15 min, respectively. In Figure 4, first derivative of TGA (DTG) was applied to obtain degradation curves, which state that after drug release, the ibuprofen degradation stage disappears, which indicates that drug release was completed while PLA/PLGA microspheres with PVA remains stable and exhibits a similar curve to blank PLA/PLGA microspheres. Figure 5 shows the SEM images of PLGA/PLA microspheres with ibuprofen after the drug release experiment in PBS media and the blank PLGA/PLA microspheres, which help us to corroborate that PLA/PLGA microspheres with PVA remains stable after the drug release.

References

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Figures

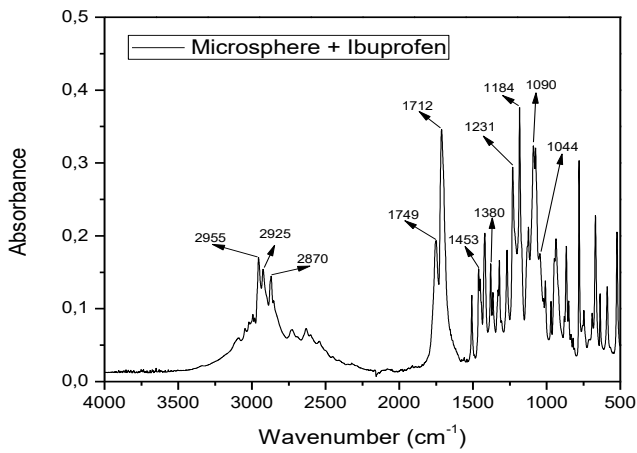


Figure 1. FTIR of PLA/PLGA microspheres

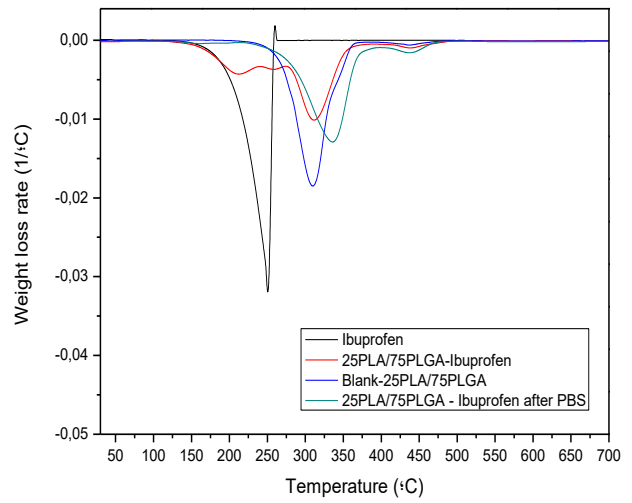


Figure 4. DTG of Ibuprofen, PLA/PLGA microspheres-Ibuprofen, PLA/PLGA microspheres-Ibuprofen after drug release experiment in PBS media and blank PLA/PLGA microspheres.

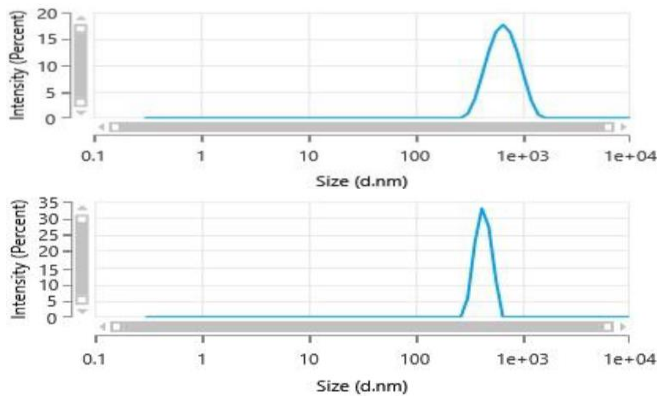


Figure 2. Comparison between the size distribution of two similar PLA/PLGA microspheres with different emulsion speed stirring. (A) 16.000 rpm. (B) 12.000 rpm.

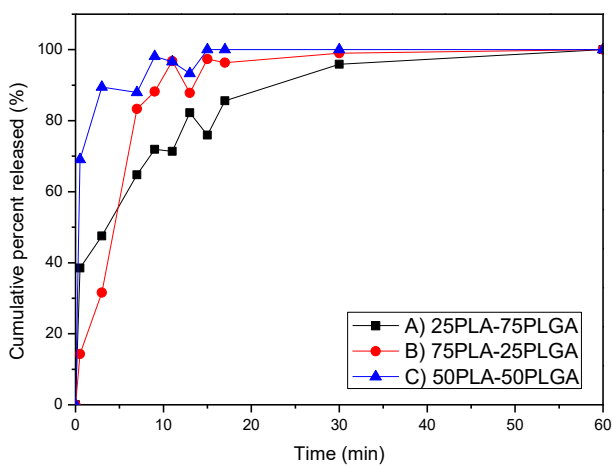


Figure 3. Comparison between the ibuprofen release profiles of PLA/PLGA microspheres with different PLA and PLGA concentrations. (A) 25%PLA and 75%PLGA. (B) 75%PLA and 25%PLGA. (C) 50%PLA and 50%PLGA.

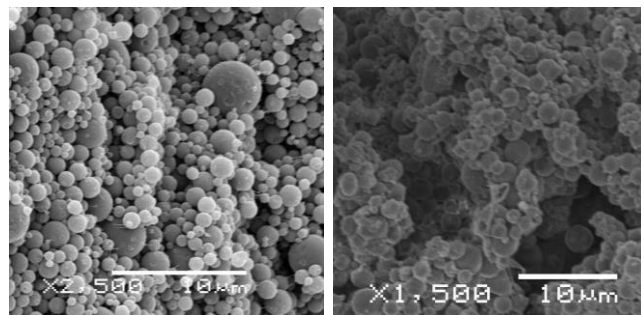


Figure 5. SEM image of blank PLGA/PLA microspheres (left) and SEM image of PLGA/PLA microspheres with ibuprofen after the drug release experiment in PBS media (right).