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ABSTRACT

The major goals of the present study were to examine the effects of the type of release medium on the resulting drug release kinetics and to get further insight into the underlying drug release mechanisms. Spherical micro and nanoparticles were prepared by a physicochemical solvent/non-solvent method with polyvinyl pyrrolidone as a surfactant and characterized with ultraviolet (UV) spectroscopy and scanning electron microscopy (SEM) before and upon exposure to various release media.

INTRODUCTION

Biodegradable nano/microparticles of poly(D,L-lactide-co-glycolide) (PLGA) and PLGA-based polymers are widely explored as carriers for controlled delivery of therapeutics such as proteins, peptides, vaccines, genes, antigens, growth factors, vitamins, etc [1-3]. Polymer degradation plays a key role in medicament release from sustained release polyester systems, therefore in order to elucidate the mechanism governing release, it appears essential to analyze the *in vitro* degradation behavior of these devices [4]. The selection of an appropriate release medium for *in vitro* tests simulating *in vivo* conditions can be very important for getting rapid feedback on the release characteristics of a specific batch.

EXPERIMENTAL

Poly(DL-lactide-co-glycolide) micro and nanoparticles without and with encapsulated ascorbic acid were prepared using a physicochemical solvent/non-solvent method as we reported in our previously work [3, 4]. The degradation of the PLGA/ascorbic acid nanoparticles and release rate of the ascorbic acid were studied for more than fifty days in a physiological solution (0.9% sodium chloride in water) or in phosphate buffered saline (PBS, one tablet dissolved in 200mL of deionized water yields 0.137 M sodium chloride, 0.01 M phosphate buffer and 0.0027 M potassium chloride) with sodium azide (0.1M solution natriumazid NaN₃) as a degradation medium. In the PBS was added 110 μ l sodium azide because sodium azide acts as a bacteriostatic. The UV measurements were performed on Perkin-Elmer Lambda 35 UV-vis Spectrophotometer in the frequency interval of 200–400 nm. The pH of the physiological solution or PBS has been measured using pH indicator strips obtained from Merck (KGaA, Germany) at various time periods to follow the acidity of the degrading medium with time. The morphology of PLGA/ascorbic acid 85/15% nanoparticles after 17 and 28 days of the degradation in phosphate buffered saline has been examined by scanning electron microscope JEOL JSM-6490LV.

RESULTS AND DISCUSSION

PLGA completely degrades within period of 8 weeks in physiological solution as a degradation medium as well as in phosphate buffered saline, fully releasing all the encapsulated ascorbic acid (Figure 1). From the image 2, we can see that during the degradation the particles were first agglomerated, then forming the film. By the end of the experiment the particles have fully degraded and there were no more traces of them in the solution.

From the figure 3 it can be noted that during the time of the degradation pH of the solution decreases as a result of the accumulation of PLGA degradation products and ascorbic acid. It could be expected that the faster degradation of the lower molar mass fraction, present in copolymer, increase the local acidity, thereby, accelerating the hydrolysis of higher molar mass species. In other words, when acid accumulation creates a local pH drop, catalytic degradation of the polymer itself occurs.

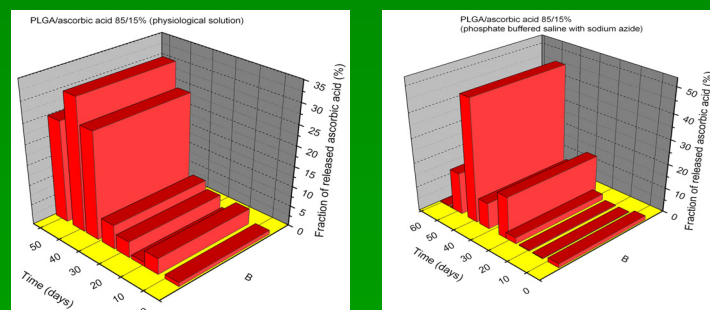
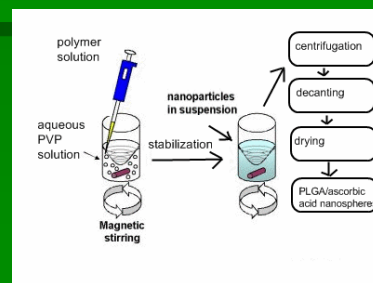


Figure 1. Release of the ascorbic acid in percentages over the period of time of the degradation in the case of a) physiological solution and b) phosphate buffered saline as a degradation medium (relative review)

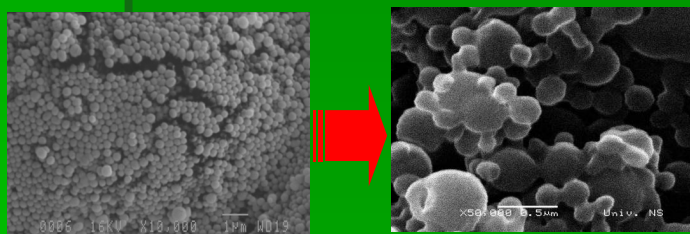


Figure 2.1 SEM images of PLGA/ascorbic acid 85/15% nanospheres before (a) and after 17 (b) and 28 days (c) of the degradation in phosphate buffered saline

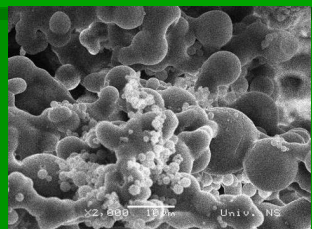


Figure 2.2 SEM images of PLGA/ascorbic acid 85/15% nanospheres after two (a) 24 (b) and 39 days (c) of the degradation in physiological solution

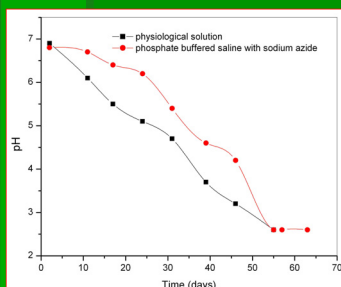


Figure 3 Changes in the pH of the degradation medium with immersion time for the PLGA/ascorbic acid 85/15% nanoparticles in the case of a) physiological solution and b) phosphate buffered saline

CONCLUSION

The release dynamics of the ascorbic acid from the polymer matrix is different when PLGA particles degrade in PBS and when they degrade in physiological solution, as a degradation medium. The ascorbic acid is released slower from the PLGA particles at the beginning, when PBS is used. This is explained with the slower change of pH solution as well as with the presence of sodium azide.

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