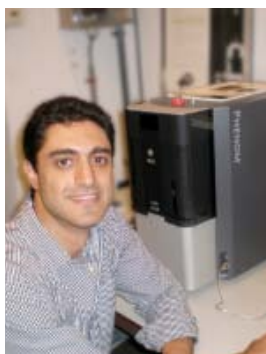


Controlled release of peptides from microparticles of hydroxylated aliphatic polyesters

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Pharmaceutical peptides and proteins have proven to be potent molecules for the treatment of a great variety of chronic and life-threatening diseases. These molecules however demand a suitable formulation for their successful delivery. The parenteral route is preferred, as other routes of administration (e.g. oral, rectal, lung) have been shown to be inefficient. Another characteristic of many peptides and proteins is that they have a short plasma and tissue half life. This leads to frequent injection schemes to maintain a therapeutic drug level. Consequently, sustained release systems would lead to less frequent injections and an improved pharmacokinetic profile as the blood and tissue levels will show fewer fluctuations over time.



A.H. Ghassemi:

"A fast and easy way to become a micro-scale photographer"

To this end, we have studied the suitability of biodegradable microparticles composed of a newly developed hydroxylated aliphatic polyester, poly(lactic-co-hydroxymethyl glycolic acid) (PLHMGA), as a controlled release system for pharmaceutical peptides/proteins, at the Department of Pharmaceutics, Utrecht University. PLHMGA microspheres loaded with different bioactive peptides and proteins were prepared by double emulsion evaporation techniques, with the size distribution ranging from 5-12 μm . A key factor in sustained release of biopharmaceutical from microspheres systems is the morphology of the microspheres.

In our early studies, based on Phenom's images, we discovered that the PLHMGA microspheres were highly porous, which led to the high burst release of peptides and proteins from microspheres (Fig.1). In order to decrease the porosity of the microspheres to prevent the burst release, some modifications were made which resulted in essentially non-porous microspheres (Fig. 2). These microspheres clearly showed a better release profile compared to porous microspheres, and the Phenom images were reliable proof of our findings.

In another study, we investigated the morphology of the microspheres during degradation step by step in physiological conditions by means of Phenom imaging (Fig. 3). The high-resolution images and ease of use, helped us to show clearly the differences in degradation of the microspheres using polymers differing in polymer composition.

Overall, the Phenom desktop scanning electron microscope is a fast and easy way to obtain valuable information regarding microsphere technology. Moreover, being able to operate the SEM in less than an hour and the easy transfer of data using a USB is a great advantage of this machine.

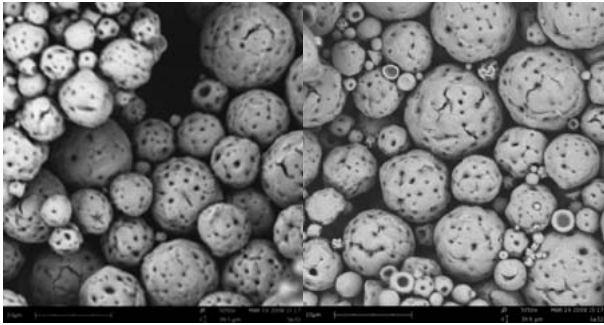


Fig. 1. Surface morphology of porous PLHMGA microspheres.

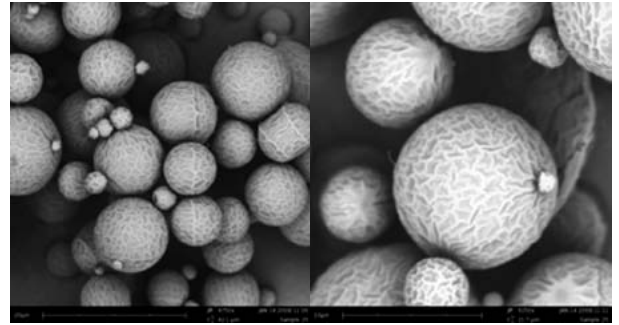


Fig. 2. Surface morphology of PLHMGA microspheres after modification of formulation.

50/50

35/65

25/75

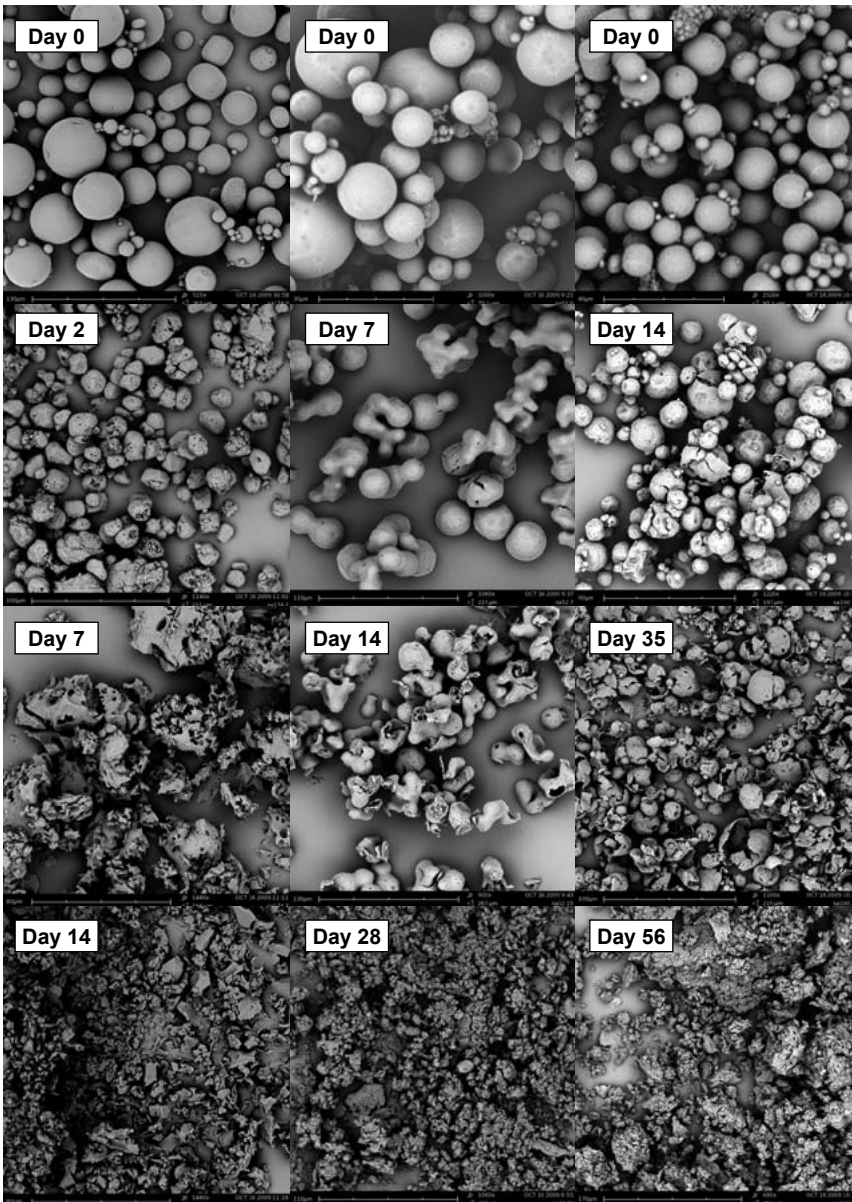


Fig. 3. Scanning electron micrographs of the PLHMGA microspheres during in vitro degradation. Microspheres were prepared from copolymers differing in copolymer composition (50/50, 65/35 and 75/25).