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Drug release mechanisms of chemically cross-linked albumin microparticles: Effect of the matrix erosion

Danielly L.A. Sitta[a], Marcos R. Guilherme[a], Edvani C. Muniz[a], Artur J.M. Valente[b], Adley F. Rubira[a,*]

[a]*Department of Chemistry, State University of Maringá, Maringá CEP 87020-900, Paraná, Brazil*

[b]*Department of Chemistry, University of Coimbra, Coimbra 3004-535, Portugal*

*Corresponding author.

E-mail address: afrubira@uem.br (A.F. Rubira).

One of the most promising areas of particles is the research and development of new pharmaceutical formulations, being that the main application is aimed towards the drug delivery. Among the various materials used in the production of nano and microparticles, there has been a considerable interest in the proteins as a starting substance for synthesis of more sophisticated release systems that may preserve the molecular structure of more potent and specific drugs [1]. Both bovine serum albumin (BSA) and human serum albumin (HSA) are used in the production of nano/microparticles [1,2] in view of their structural similarity that corresponds to 75% of the homologous sequence. BSA is more suitable for in vivo tests due to its lower cost.

This work aimed at producing protein microparticles from BSA using a hydrochloric emulsion for uses in drug delivery systems. Vitamin B12 (Vit-B12) was used as the model drug. To obtain such a system, BSA was modified with maleic anhydride (MAy) in water, because only a small number of proteins may sustain dissolution in an organic medium without their molecular recognition properties being lost. The idea was to use the vinyl bonds in functionalized BSA (BSAMAy) as a radical cross-linking/polymerization approach for reaction with *N*, *N*-dimethylacrylamide (DMAAm) in the emulsion. The microparticles produced at 15 min of stirring without PVA showed the best results in terms of size, homogeneity, and sphericity (Fig. 1a). In such a case, BSA played a role as a surface active agent, replacing PVA. For longer stirring times, BSA was unable to act as an emulsifier. These microparticles showed an uncommon release profile, consisting in a two-step release mechanism, at the pH range studied (Fig. 1b). Considering that a two-step release mechanism is occurring, the experimental data were adjusted by applying modified power law and Weibull equations in order to describe release mechanism n and release rate constant k, respectively. Each one of the release stages was related to a specific value of n and k. The second stage was driven by a super case II transport mechanism, as a result of diffusion, macromolecular relaxation, and erosion. A third model, described by Hixson–Crowell, was used to confirm the erosion mechanism.

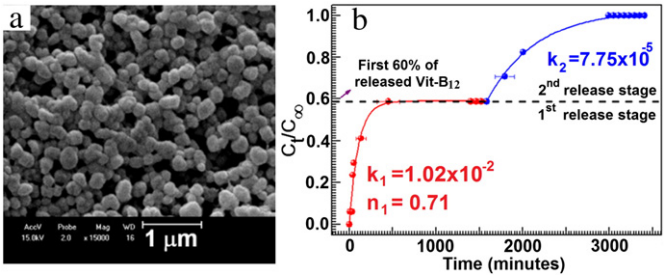

Fig. 1. (a) SEM image of BSA microparticles produced at 15 min of stirring, without PVA. (b) Time-dependent release curve of Vit-B12 from the albumin microparticles at 37 °C for pH 2.

Keywords: albumin, drug delivery, emulsion, erosion, microparticles, drug release kinetics

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Antibacterial ciprofloxacin hydrochloride incorporated PVA/regenerated silk fibroin nanofibers composite for wound dressing applications

Ahmed A. El-Shanshory[a,b], Weiming Chen[b], Hany A. El-Hamshary[c], Salem S. Al-Deyab[c], Xiumei Mo[b,*]

[a]*College of Textiles, Donghua University, Shanghai 201620, China*

[b]*College of Chemistry, Chemical Engineering and Biotechnology, Donghua University, Shanghai 201620, China*

[c]*Department of Chemistry, College of Science, King Saud University, Riyadh 11451, Kingdom of Saudi Arabia*

*Corresponding author.

E-mail addresses: shansho_medo@yahoo.com (A.A. El-Shanshory), xmm@dhu.edu.cn (X. Mo).

In order to avoid the harmful effects of organic solvents, many water soluble polymers such as polyvinyl alcohol (PVA), polyethylene oxide (PEO), silk fibroin (SF) have been used to fabricate green, Eco friendly electrospun nanofibers for biomedical applications. On the other hand SF is an attractive natural fibrous protein, which has been used for various biomedical applications including tissue

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engineering and drug delivery, due to its biocompatibility, biodegradability, low inflammatory response, good oxygen and water vapor permeability [1]. Here, we designed a wound dressing mat based on PVA and SF, in which an antibacterial drug ciprofloxacin hydrochloride (CipHCl) which is one of the most widely used antibiotics for wound healing has been incorporated [2].

In this study, CipHCl has been successfully incorporated into the PVA/SF nanofibers composite via an electrospinning technique by using water as a solvent. Electrospun PVA/SF/CipHCl composite nanofibers were stabilized by heating in an oven at 155 °C for 5 min. Incorporation of CipHCl into electrospun nanofibers was confirmed by SEM (Fig. 1) and FT-IR spectra. Further the mechanical properties test illustrated that the addition of CipHCl enhanced the mechanical properties of PVA and PVA/SF nanofibers. The antibacterial activities against *Escherichia coli* (*E. coli*) (Gram negative) and *Staphylococcus aureus* (*S. aureus*) (Gram positive) organisms were evaluated by disk diffusion method and results suggested that electrospun PVA/CipHCl and PVA/SF/CipHCl composite nanofibers showed a remarkable antibacterial activity.

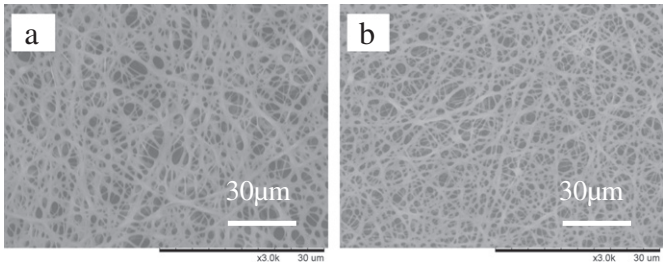

Fig. 1. SEM images of PVA/SF (a) and PVA/SF/CipHCL (b) after heat treatment.

Keywords: electrospinning, poly(vinyl alcohol), silk fibroin, wound dressing, ciprofloxacin hydrochloride

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Cell laden and patterned chitosan microgel for micro-scale tissue engineering

Baoqiang Li[a,b], Lei Wang[a,b], Jinghao Guo[a,b], Feng Xu[c], Daqing Wei[a,b], Yujie Feng[a,b], Yu Zhou[a,b]
[a]*Institute for Advanced Ceramics, Harbin Institute of Technology, Harbin 150001, China*
[b]*State Key Laboratory of Urban Water Resource and Environment, Harbin Institute of Technology, Harbin 150001, China*
[c]*Bioinspired Engineering and Biomechanics Center, Xi'an Jiaotong University, Xi'an 71004, China*
E-mail address: libq@hit.edu.cn (B. Li).

Biodegradable and cell laden polymer microgels acting as functional building blocks for micro-scale tissue engineering have potential application in the construction of complex structures like native organs and tissue [1,2]. Thermal sensitive chitosan/β-glycerol phosphate allows cell encapsulation during gelation, however the gelation is slow and there is no way to achieve patterned hydrogels. To in situ encapsulate cells during gelation and to fabricate the chitosan microgel with on-demand patterns, UV crosslinkable and water soluble chitosan methacrylic amide (Chi-MA) was synthesized via N site specific acylation. The substitution degree was in the range of 10%–50% depending on the molar ratio of anhydride and amine groups. 1.5 wt.% Chi-MA with 15.6% substitution degree was dissolved in a cell culture medium, and 0.05 wt.% FITC-labeled dextran was incorporated for fluorescent images of patterned microgels. The patterned chitosan microgel with on-demand pattern of square, circle, arc and concentric ring were fabricated by UV photolithography with a short UV exposure time (20–40 s) (Fig. 1A), the matching degree of patterned microgels was as high as 94%. NIH/3 T3 cells are in situ encapsulated in Chi-MA microgel with concentric patterns to mimic the structure of the osteon (Fig. 1B). Cell viability in Chi-MA microgel was maintained as high as 95%, and proliferated cells are guided to form specific patterns and formed networks in the microgel (Fig. 1C), which provides an easy and efficient method for the cell encapsulation in patterned chitosan hydrogel. UV photolithography allows gelation of UV crosslinkable chitosan hydrogel with on-demand pattern and in situ cell encapsulation during chitosan hydrogel fabrication. Cell laden and patterned chitosan microgel analogous to the basic unit of the biological system can be adopted from the polysaccharide based building blocks for bottom up assembly of micro-scale tissues engineering with the aim to construct complex organs or tissue.

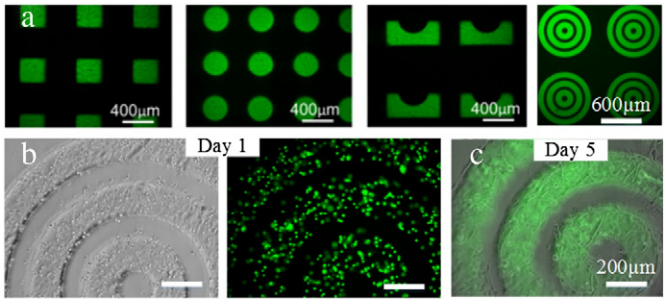

Fig. 1. Cell laden and patterned chitosan microgel. (A) Patterned chitosan microgel with square, circle, arc and concentric rings. (B) Cells were in situ encapsulated in patterned concentric rings chitosan microgel with cell viability as high as 95%. (C) Cell proliferation and formation of network in patterned chitosan microgel.

Keywords: UV crosslinkable hydrogel, cell patterning, patterned hydrogel, chitosan microgel

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