

Macroporous structures based on biodegradable polymers—candidates for biomedical application

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Abstract: New hybrid cryogels comprising natural polymers (free atelocollagen or atelocollagen mixed with a hyaluronic acid derivative) and a synthetic polyester—poly(ϵ -caprolactone)—were successfully developed by a cryogenic treatment and a subsequent freeze-drying step. Systematic studies on the effect of preparation conditions (reaction mixture composition, total concentration of the feed dispersion, and freezing regime) on cryogelation efficiency were conducted. The degree of cross-linking and the morphology of the obtained materials were analyzed using differential scanning calorimetry (DSC), Fourier transform infrared spectroscopy (FTIR) and (environmental) scanning electron microscopy (ESEM/SEM) techniques. Considering their possible biomedical application, the developed macroporous hydrogels were also inves-

tigated in terms of swelling behavior and hemo/biocompatibility. The produced hydrogels had an uniform interconnected open porous structure with a porosity of up to 95% and pores size in the range of 83–260 μm . All obtained cryogels were elastic, mechanically stable, with a superfast swelling kinetics. *In vitro* hemocompatibility assay gave hemolysis ratios (HRs) lower than 0.5%, which is below the permissible limit of 5%. The *in vivo* tolerance tests performed by implantation of cryogel specimens into Wistar rats proved their biocompatibility. © 2013 Wiley Periodicals, Inc. *J Biomed Mater Res Part A*: 00A:000–000, 2013.

Key Words: cryogels, atelocollagen, hyaluronan, poly(ϵ -caprolactone), biocompatible materials

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INTRODUCTION

3D structures based on biopolymers, mainly hydrogels, form a versatile class of materials with widespread application in regenerative medicine, cosmetics, and pharmaceuticals. Between the challenges in achieving the envisaged performances the choice of the cross-linking alternative and the selection of the components for gel formation are the most important. An often used strategy in generating such biomaterials with appropriate characteristics consists in combining the biopolymers biomimetic properties with the mechanical tailoring of the synthetic polymers.¹ In this context, earlier reported studies focused on the development of ternary atelocollagen:hyaluronan:poly(ϵ -caprolactone) (AteCol:HA:PCL) hydrogels in dense films or as sponges. It was demonstrated that the specific characteristics of each component may be used to produce materials with unique structure and properties in a controlled manner.²

The present article concentrates on cryogels with a similar ternary composition, aiming to improve product cleanliness, mechanical properties, and processability, without affecting the collagen triple helix. The approach exploits the cell-binding properties of collagen, the immunosuppressive properties of HA, the structural properties of PCL, and the specific advantages offered by cryogelation to provide possible favorable substrates for cell growth.

Cryogels, a new class of 3D materials, consist in a highly interconnected open macroporous network, characterized by a good mechanical strength, elasticity, and the ability to retain the cryo-mold shape.^{3,4} They are obtained at subzero temperatures, through the formation of both physically and covalently cross-linked homogeneous or heterogeneous polymer networks, using moderately frozen solutions of monomeric or polymeric precursors.^{3–5} Due to their characteristics, cryogels may have advantages in future

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