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Collagen-Based Hybrid 3-D Matrices

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***Abstract*—Attempts to obtain collagen-based biomimetic 3D structures with possible use in the biomedical domain (scaffolds in tissue engineering, component of wound dressing) are presented. Different preparation approaches were applied and the resulted materials were comparatively characterized pointing on advantages/drawbacks of the corresponding preparative alternative. Aiming the material characteristics control in order to achieve the targeted performances required by the application domain, computer aided material selection facilities were considered. Development of supervised artificial network for appropriate composition selection was proved to be an important, efficient tool for control and prediction even for complex multicomponent materials such as those here considered.**

Keywords—biopolymers, poly(ε-caprolactone), tridimensional matrix, artificial neural network, biomedical applications

I. INTRODUCTION

Combination strategy - i.e. combining different, often incompatible materials, modifying them by both covalent and noncovalent bonding, applying new and classical approaches for materials engineering according final use needs - is one of the main trends in the last decade research enabling progress in biomedical device development in order to achieve the required performances (physic-chemical and biological properties, processing facility) [1]. Envisaging the development of a rational design of an appropriate 3D system for further use as a scaffold or a component of wound dressings our choice was such a complex, combined system, involving inclusion of natural (collagen, hyaluronan derivative) and synthetic polymers (poly(ε-caprolactone) - PCL), integrated in a 3D structure by multiple cross-linking (e.g. by physical and chemical methods) [2-4]. Collagen and hyaluronan were selected due to biomimicry reasons, both being main components of the extracellular matrix (ECM) [5]. PCL, a synthetic, biodegradable polyester with low in vivo degradation kinetics, was used here as a bifunctional derivative with cross-linking function, to increase multicomponent system stability [6]. Applying different approaches the final biomaterials were obtained in form of sponges, dense films or macroporous matrix.

Here, the obtained synthesis and characterization data are comparatively presented, pointing on the advantages and drawbacks of each preparative alternative, in correlation with the envisaged application, underlying the versatility offered by combination strategy in terms of complex materials, with tuned properties development. The neural modeling of the degradability of the complex developed systems was performed aiming to use the artificial neural network. algorithm as an alternative solution in the design of multicomponent biomaterials.

I. EXPERIMENTAL

A. Materials

Poly(ε-caprolactone) diisocyanate (PCL-DI) and type I atelocollagen (AteCol) were obtained according literature [2, 7]. Dimethylsilanediol hyaluronate (DMSHA) solution (commercial form, DSH−CN) were supplied by EXSIMOL S. A. M. (Monaco). 1-ethyl-3-(3-dimethylaminopropyl) carbo-diimide (EDC), N-hydroxysulfosuccinimide (NHS), Triton X-100, 2,4,6-trinitrobenzenesulfonic acid solution (TNBS, 1M) and dimethylsulfoxide (DMSO) were purchased from Fluka (Germany). All other reagents and solvents (ethanol, acetone) were commercially available and were used without further purification. Bidistilled water was used for all experiments.

B. Sample preparation

The porous, macroporous and dense matrices were prepared according literature [2-4]. Different preparative protocols were applied, i.e:

1. lyophilization of an acidic AteCol dispersion followed by cross-linking by EDC/NHS system, completed with long-range cross-linking with PCL-DI, to yield collagen–based sponges;
2. casting on a bend dish of the homogenized dispersion resulted by AteCol, DMSHA and PCL-DI mixing, followed by dehydration by slow drying under vacuum, in order to obtain dense films;
3. application of appropriate cryogenic treatment to similar biopolymers/PCL-DI mixtures, followed by UV irradiation of the formed cryogel and subsequent freeze-drying, to realize macroporous matrices.

The adopted code was CHxPy-z, **n**, where x represents wt% DMSHA, y is wt% PCL-DI, z represents the irradiation duration (min), and C, H, and P are the abbreviations used for AteCol, DMSHA, and PCL, while n is the code for the selected protocol (as before mentioned), respectively.

C. Characterization

Attenuated total reflection Fourier transform-infrared (ATR-FTIR) spectra were recorded on a Vertex 70 (Bruker) spectrophotometer. The cross-linking efficiency was evaluated by (a) determination of the free amino group content of the investigated samples (using the 2,4,6-trinitrobenzenesulfonic acid (TNBS) assay [8]), (b) by calculus of $A_{1660/1490}$ ratio (related to collagen modification/crosslinks [9]), (c) by investigation of thermal

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