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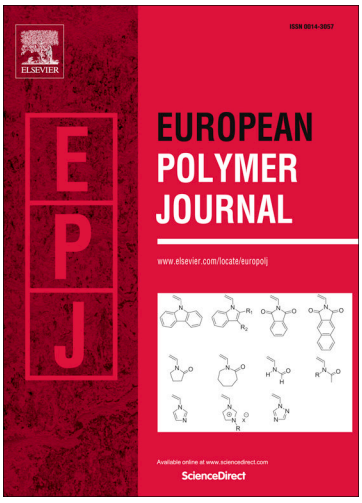

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Calcium phosphate/polyvinyl alcohol composite hydrogels: A review on the freeze-thawing synthesis approach and applications in regenerative medicine

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Abstract

Composite biomaterials are of great interest in tissue engineering and regenerative medicine. Composites partially exhibit the properties of their starting materials but, through rational design, they can be endowed with synergistic effects, overcoming the limitations of the single components. Calcium phosphate/polyvinyl alcohol (CaP/PVA) composites are archetypical examples of composite biomaterials, where a soft elastic biologically inert gel is combined with a bioactive inorganic phase, radically improving the mechanical properties. The combination allows engineering a material which better resembles the tissue architecture, for example, osteochondral defects, where organic-inorganic interfaces and gradient properties are present. The combination of components with opposite properties such as polyvinyl alcohol (PVA) and calcium phosphates (CaP) for creating synergistic properties is a grand challenge for the material engineer, where the know-how on PVA preparation must be adapted to the necessity of incorporating a phase with the appropriate size, aspect ratio, chemical composition, homogeneity or even pre-determined composition gradients. In this review, we report how these design challenges were overcome and how different design parameters involved in CaP/PVA influence each other. The review is organized as follows. First, the general properties of organic/inorganic composites and PVA hydrogels are briefly summarized. Then, CaP/PVA composites are described according to their preparation methods, discussing how parameters such as polymer deacetylation degree, tacticity, molecular weight, freeze-thawing parameters, CaP content or CaP addition or *in situ* preparation modality influence the composite's properties such as friction, boundary lubrication, porosity, and osteointegration. Finally, open research questions and future and desirable developments are given.

Keywords: Calcium phosphate, Polyvinyl alcohol, Nanocomposite, Hydrogel, Tissue engineering, Freeze-thawing

1. Introduction

Musculoskeletal conditions are the second greatest cause of disability globally [1]. About 24% of people in the European Union are subjected to the long-term treatment of musculoskeletal diseases [2]. The average number of knee and hip replacement surgeries in Europe is approximately 115 (in 2006) and 175 (in 2007) cases per 100000 people, and these numbers continue to rise rapidly [2]. Furthermore, the number of years lived with disability due to the bone fractures is higher than those for other noncommunicable diseases [3]. Accordingly, new therapeutic solutions directed to the appropriate treatment or replacements of the damaged tissues with innovative biomaterials are prospected.

PVA is one of the most widely used polymers in biomedical engineering [4] and pharmaceutical technology [5] due to its biocompatibility (i.e. compatibility with living tissues by not being toxic, injurious or physiologically reactive and not causing negative immunological response) [6], the ability to form crosslinked structures without the incorporation of toxic