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Towards the synthesis of an Mg-containing silicate glass–ceramic to be used as a scaffold for cementum/alveolar bone regeneration

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Abstract

The gradual destruction of periodontal tissue and in particular the reduction of alveolar bone height which can ultimately lead to tooth loss is a common problem in patients suffering from periodontal disease. The aim of the present work was to investigate the sol–gel synthesis and characterization of a family of new Mg-containing bioactive silicate glasses for applications in cementum/alveolar bone regeneration. Their microstructural, biological and mechanical characteristics were optimized for the fabrication of functional bioceramic scaffolds using the foam replica technique. The optimal glass composition for periodontal tissue replacement was found to contain 60 mol% SiO_2, 30 mol% CaO and 10 mol% MgO. After sintering, this composition had enhanced mechanical properties combined with the desired apatite-forming ability, which was tested in simulated body fluid (SBF) for up to 5 days. *In vitro* analysis revealed positive effects of these scaffolds on bone marrow stromal cells.

Keywords: A. Powders: chemical preparation; D. Glass–ceramics; D. Silicate; C. Hardness; E. Biomedical applications

1. Introduction

Periodontitis is one of the most common diseases in humans, affecting in its most severe form, approximately 10–15% of the population [1]. It is characterized by progressive destruction of the tooth-supporting apparatus [2,3], the periodontium, which could be regarded as one of the most complex dental structures, particularly related to architecture and function [4]. The periodontium consists of two soft (gingival and periodontal ligaments) and two hard (alveolar bone and cementum) tissues. Both alveolar bone and cementum are highly calcified tissues consisting mainly of hydroxyapatite ($Ca_5(PO_4)_3(OH)$) [3,5]. The mineral component of cementum presents a relatively low degree of crystallinity, which facilitates the adsorption of various elements, such as magnesium (Mg), indicating the compositional resemblance of cementum to bone tissue [5,6].

Mg-containing bioactive glasses and glass–ceramics have attracted the interest of the scientific community because of their improved mechanical properties [7] and the controlled rate of biodegradation [8]. Additionally, magnesium plays a fundamental role in cellular processes [9,10] and skeletal metabolism [11,12]. It is one of the most important mineral elements in the human body, with approximately half of the total physiological magnesium stored in bony tissues [13]. Furthermore, Huang et al. [14] compared akermanite ($Ca_2Mg(Si_2O_7)$) and β-tricalcium phosphate (β-TCP) in their ability to induce differentiation of human mesenchymal stem cells, showing that the release of Si and Mg significantly facilitated stem cell proliferation and differentiation.

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Simultaneously, the possibility of synthesizing these biomaterials using a variety of methods, including a sol–gel technique, enables the development of materials with controlled porous structure and high surface energy [15].

Novel scientific approaches in bone tissue engineering combine the application of Guided Tissue Regeneration (GTR) with an artificial Extracellular Matrix (ECM), via scaffold materials which are loaded with cells and signaling molecules such as growth factors. The cell can be cultured *in vitro* on the scaffold and subsequently, be implanted into tissue defects to induce and direct the growth of new tissue [16,17]. Bone tissue regeneration based on polymeric scaffolds encounters several challenges. Firstly, the acidic products of some polymers (such as poly(lactic acid), poly(glycolic acid), and their copolymer, PLGA) may exert adverse effects on dental tissue formation [18]. Secondly, the nutrient delivery and metabolic waste removal inside a scaffold are often limited, which may affect sequential cell differentiation [19]. Finally, non-specific inflammatory responses of the host tissue to almost all polymer materials are often inevitable when they are placed *in vivo* [20]. Concerning cementum regeneration, Grzesik et al. [21] have proposed that the key factor to achieve periodontal regeneration is the successful formation of the acellular cementum. However, according to a recent review paper [2], the formation of an acellular cementum and the restoration of the attachment of the connective tissue to that cementum have yet to be demonstrated in a reproducible fashion.

Current data concerning the use of scaffolds in periodontal tissue regeneration are far from being sufficient to demonstrate successful tissue-engineering therapeutics. Consequently, there is a need for the development of advanced biomimetic scaffold materials, which are versatile enough to be targeted for tooth-specific applications and capable to drive the growth and functional differentiation of stem/progenitor dental cells into mature organized periodontal tissue in a controlled manner. As a materials science contribution to the field of cementum/alveolar bone regeneration, the aim of the present study was to investigate the sol–gel synthesis and characterization of a family of Mg-containing bioactive silicate glasses varying in both network formers and modifiers. These glasses were subsequently optimized regarding their microstructural, biological and mechanical characteristics, in order to serve as starting materials for the fabrication of functional bioceramic scaffolds by the foam replica technique.

2. Experimental procedure

2.1. Synthesis of the Mg-containing glasses

All glasses were synthesized by the sol–gel technique as reported by Saravanapavan et al. [22,23] for the synthesis of S70C30 glass (containing 70 mol% SiO_2 and 30 mol% CaO). In detail, the bioactive glass compositions were prepared by mixing DI H_2O, 2 N HNO_3 and tetraethoxysilane (TEOS) using molar ratios H_2O/TEOS of 12:1 and volume ratios H_2O/HNO_3 of 6:1, while the amounts of magnesium nitrate hexahydrate ($Mg(NO_3)_2 \cdot 6H_2O$) and calcium nitrate tetrahydrate ($Ca(NO_3)_2 \cdot 4H_2O$) were calculated accordingly and added in the composition. The glass compositions shown in Table 1 were synthesized. All Mg-containing materials can be categorized in two groups according to their composition; the first (group A) includes the glasses that were produced by lowering the amount of CaO in the 70S composition (70S10Mg and 70S20Mg) and the second group includes the glasses that were produced by lowering the amount of SiO_2 in the 70S composition (60S10Mg and 50S20Mg). Aging, drying and chemical stabilization of the prepared sols were carried out in a muffle furnace (Nabertherm, L9/12) according to Saravanapavan et al. [22].

Table 1
The developed bioactive glass compositions (in mol%).

Oxide	Sample				
	Group A		70S	Group B	
	70S10Mg	70S20Mg		60S10Mg	50S20Mg
SiO_2	70	70	70	60	50
CaO	20	10	30	30	30
MgO	10	20	–	10	20

2.2. Characterization of the Mg-containing glasses

All glasses were characterized by Thermogravimetric-Differential Thermal Analysis (TG-DTA), performed with a Setaram thermogravimetric-differential thermal analyzer SETSYS TG-DTA 16/18, with heating rate 10 °C/min in a dry air atmosphere and furnace cooling. The heating was performed up to 1200 °C and according to the thermogram, the glasses were heated at various temperatures in order to evaluate the optimum sintering temperature, based on the developed crystalline phases, apatite-forming ability and hardness.

2.2.1. Structural characterization

The crystal structure of the material before and after heat treatment was evaluated by Fourier Transform Infrared Spectroscopy (FTIR) and X-Ray Diffractometry (XRD). FTIR transmittance spectra were obtained using an FTIR spectrometer (Nicolet, USA) in the MIR region (4000–400 cm^{-1}) with a resolution of 4 cm^{-1} by the KBr pellet technique. The XRD measurements were carried out using a D8 ADVANCE X-ray diffractometer (Bruker, Madison, US) equipped with a VANTEC-1 detector. The spectra were recorded in the 2Theta range using Cu Kα radiation (λ=.15406 nm) in the range 20–60° with a step size of .014 °/step and accumulation time of 3.0 s per step. The synthesized materials were powdered and dispersed in ethanol. Then the solution was dripped on off-axis cut, low background silicon wafers (Bruker AXS, Germany). All spectra were background corrected and $K\alpha_2$ was stripped mathematically.

2.2.2. In vitro apatite-forming ability evaluation

The apatite forming ability of the materials was assessed by immersion of sintered pellets for 1, 3 and 5 days in Simulated