Available online at www.sciencedirect.com

ScienceDirect

Ceramics International 41 (2015) 7241–7251

CERAMICS INTERNATIONAL

www.elsevier.com/locate/ceramint

Review paper

Effect of ion substitution on properties of bioactive glasses: A review

Sayed Mahmood Rabiee[a], Neda Nazparvar[a], Misaq Azizian[a], Daryoosh Vashaee[b], Lobat Tayebi[c,d,*]

[a]Department of Materials Engineering, Babol University of Technology, Babol, Iran
[b]Electrical and Computer Engineering Department, North Carolina State University, Raleigh, NC 27606, USA
[c]School of Materials Science and Engineering, Helmerich Advanced Technology Research Center, Oklahoma State University, Tulsa, OK 74106, USA
[d]Department of Developmental Sciences, Marquette University School of Dentistry, Milwaukee, WI 53233, USA

Received 24 September 2013; received in revised form 21 February 2015; accepted 25 February 2015
Available online 6 March 2015

Abstract

Bioactive glasses and glass-ceramics have recently found key applications in biomedicine, mainly for bone repair and replacement. Recent developments in the field of tissue engineering have re-invigorated the quest to enhance the physical and biomedical effectiveness of bioactive glasses and glass-ceramics by incorporation of different elements into the composition of these materials. Although most elements are included in the bioactive glass for the therapeutic benefits (e.g., Ag and Sr), they influence the structure and bioactivity of the glass. This review systematically discusses the influence of the addition of silver (Ag), magnesium (Mg), strontium (Sr), zinc (Zn), aluminum (Al), potassium (P), fluoride (F) and zirconia (ZrO_2) elements on the chemical, physical and therapeutic properties of bioactive glasses and glass-ceramics, which are expected to play an important role in the future of bone regenerative medicine. This article describes where these dopant ions fit into the glass structure and how these affect the delivery and properties of the glass as a whole.

Keywords: D. Glass-ceramics; Bioactive glass; Ion substitution

Contents

1. Introduction

Bioceramics, as an essential group of biomaterials, have recently found wide applications in medicine [1–5]. Among

*Corresponding author at: Department of Developmental Sciences, Marquette University School of Dentistry, Milwaukee, WI 53233, USA. Tel.: +1 414 288 8383.
E-mail address: lobat.tayebi@marquette.edu (L. Tayebi).

http://dx.doi.org/10.1016/j.ceramint.2015.02.140
0272-8842/

various kinds of bioceramics, glass and glass-ceramics, in the SiO_2–CaO–P_2O_5 system, are specifically beneficial for repair and replacement of diseased and damaged bone tissues [6,7]. Moreover, use of bioactive glass in hybrid structures with other ceramics, polymers and hydrogels becomes a fast growing trend in bone regeneration research [8,9]. The first bioactive glass (45S5 Bioglass, 46.1% SiO_2, 24.4% NaO, 26.9% CaO and 2.6% P_2O_5, in mol%) was made by Hench and co-workers in the 1960s [10]. This bioactive glass was the first material that formed an interfacial bond with host tissue and did not become surrounded by fibrous tissue after implantation [10,11]. Bioactive glass particulates have been used in clinical applications since 1985 [12]. Once implanted in the body, bioactive glass can react to the physiological fluids and form a strong chemical bond with bones. Its bioactivity is associated with the formation of the hydroxyl carbonated apatite (HCA) layer on its surface, similar to the bone mineral. The HCA crystals bond to layers of collagen fibrils produced at the interface by osteoblasts. The bonding of the hydroxyapatite (HA) layer to collagen creates a strong chemical interface [10,11]. The HCA layer forms as a result of a rapid sequence of chemical reactions on the surface of the implant when in contact with body fluid [13,14]. There are five proposed reaction stages that lead to the rapid release of soluble ionic species and the formation of a high surface area hydrated silica and polycrystalline HCA bi-layer on the glass surface [1]:

- Stage 1: rapid exchange of Na^+ and Ca^{2+} with H^+ or H_3O^+ from solution, causing hydrolysis of the silica groups, which creates silanols (Si–OH), e.g.,

  $$Si\text{–}O\text{–}Na^+ + H^+ + OH^- \rightarrow Si\text{–}OH^+ + Na^+(aq) + OH^-$$

  Ion exchange is diffusion controlled at 1/2 dependence. The pH of the solution increases as a result of H^+ ions in the solution being replaced by cations.

- Stage 2: stage 1 increases the hydroxyl concentration of the solution, which leads to attack of the silica glass network. Soluble silica is lost in the form of $Si(OH)_4$ to the solution, resulting from the breaking of Si–O–Si bonds and the continued formation of silanols at the glass solution interface:

  $$Si\text{–}O\text{–}Si + H_2O \rightarrow Si\text{–}OH + OH\text{–}Si$$

- Stages 3–5: condensation and repolymerization of the silanols groups are then thought to occur, leaving a silica-rich layer on the surface, depleted in alkalis and alkali-earth cations (stage 3). Ca^{2+} and PO_4^{3-} groups then migrate to the surface through the silica-rich layer and from the surrounding fluid, forming a CaO–P_2O_5 rich film on top of the silica-rich layer (stage 4). The CaO–P_2O_5 film crystallizes as it incorporates OH^- and CO_3^{2-} anions from solution to make a mixed carbonated hydroxyl apatite HCA layer.

Bioactive glasses and glass-ceramics can be synthesized by both melting and sol–gel methods, although the latter is preferred because of its higher compositional range of bioactivity and higher surface area that results in better binding to the living tissues [15]. For producing bioactive glass products, different techniques have been employed, such as electrospinning [16–18], laser-spinning [19], flame spray [20–23], microemulsion [24], polymer foam replication [25], sol–gel foaming [26], gel cast foaming [27], and 3D printing [28].

High solubility is the major disadvantage of bioactive gasses. It has been suggested that most of the released ions might be transported away from the surroundings of the implantation site by body fluid before new bone forms [12]. In addition, owing to low fracture toughness, glasses are brittle materials and are easily cracked [29]. When converting glass into glass-ceramic, the fracture toughness commonly increases. Glass-ceramic materials, prepared by controlled crystallization of glasses, have a variety of established uses because of their excellent properties, such as uniform reproducible fine grain microstructure [30].

Since the discovery of the first bioactive glass [10], several other glass and glass-ceramic compositions have been developed to improve the properties and clinical abilities of traditional bioactive glass. One trend is the incorporation of different elements into the composition of these bioactive glasses and glass-ceramics to enhance their physical characteristics and therapeutic benefit. Ceravital, which precipitates apatite in Na_2O–K_2O–MgO–CaO–SiO_2–P_2O_5 glass; glass-ceramic A–W, which precipitates apatite and wollastonite in MgO–CaO–SiO_2–P_2O_5 glass; Bioverit, which precipitates apatite and phlogopite in Na_2O–MgO–CaO–Al_2O_3–SiO_2–P_2O_5–F glass implant, which precipitates apatite and wollastonite in Na_2O–K_2O–MgO–CaO–SiO_2–P_2O_5–CaF_2 glass; and glass-ceramics that precipitate canasite in Na_2O–K_2O–CaO–CaF_2–P_2O_5–SiO_2 glass are the glass-ceramics that are currently of the greatest interest. Among these, glass-ceramic A–W has been most widely used clinically [31].

Hoppe et al. [32] recently reviewed the biological response of human cells to different ionic dissolution products from bioactive glasses. However, in this article, we focused on presenting the recent progress in the use of several additive ions, silver (Ag), magnesium (Mg), strontium (Sr), zinc (Zn), aluminum (Al), fluoride (F), potassium (P) and zirconia (ZrO_2), to influence the material and therapeutic properties of bioactive glass.

2. Silver-bioactive glass

Any use of implants is associated with a risk of adherence and colonization of bacteria on the surface of the implant, which can lead to failure of the implant and bacterial infections [33]. The consequences of implant infections are serious, often leading to revision surgery and prolonging time of hospitalization [34]. A broad spectrum of pathogens can be found at implant sites, including *Pseudomonas aeruginosa*, *Escherichia coli*, *Staphylococcus aureus* and *Staphylococcus epidermidis* [33].

The antimicrobial properties of the silver ion have been demonstrated since ancient times by Mediterranean and Asiatic cultures [34]. The recent focus on the development of silver for various applications has been centered on this material's antibacterial activity [35,36]. The antibacterial bioactive