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# ACCEPTED MANUSCRIPT

### Mesoporous Silica-Based Bioactive Glasses for Antibiotic-free Antibacterial Applications

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#### Abstract

Bioactive glasses (BGs) are being used in several biomedical applications, one of them being as antibacterial materials. BGs can be produced via melt-quenching technique or sol-gel method. Bactericidal silver-doped sol-gel derived mesoporous silica-based bioactive glasses were reported for the first time in 2000, having the composition 76SiO<sub>2</sub>-19CaO-2P<sub>2</sub>O<sub>5</sub>-3Ag<sub>2</sub>O (wt%) and mean pore diameter as 28.2±2.6 nm. This review paper discusses studies carried out exploring the potential antibacterial applications of drug-free mesoporous silica-based BGs. Bioactive glasses doped with metallic elements such as, silver, copper, zinc, cerium and gallium are the point of interest of this review, in which SiO<sub>2</sub>, SiO<sub>2</sub>-CaO and SiO<sub>2</sub>-CaO-P<sub>2</sub>O<sub>5</sub> systems are included as the parent glass compositions. Key findings are that silica-based mesoporous BGs offer a potential alternative to the systemic delivery of antibiotics for prevention against infections. The composition dependent dissolution rate and the concentration of the doped elements affect the antibacterial efficacy of BGs. A balance between antibacterial activity and biocompatibility is required, since a high dose of metallic ion addition can cause cytotoxicity. Typical applications of mesoporous BGs doped with antibacterial ions include bone tissue regeneration, multifunctional ceramic coatings for orthopaedic devices and orbital implants, scaffolds with enhanced angiogenesis potential, osteostimulation and antibacterial properties for the treatment of large bone defects as well as in wound healing.

Keywords: Mesoporous; Antibacterial; Bioactive glass; Sol-gel technique; Antibiotic-free

### **1. Introduction**

The first bioactive glass (BG) was invented by Larry Hench at the University of Florida in 1969 [1]. This bioactive glass has a composition of  $46.1SiO_2$ -  $24.4Na_2O$ -26.9CaO- $2.6P_2O_5$  (mol%), later termed as Bioglass<sup>®</sup>45S5, and exhibited as a key property the formation of a bond with bone so strong that it could not be removed without breaking the bone [1] [2]. From a compositional viewpoint, bioactive glasses can be basically divided into three groups, depending on the representative network former oxide present in the formulation, i.e., SiO<sub>2</sub>-based (silicate), B<sub>2</sub>O<sub>3</sub>-based (borate) and P<sub>2</sub>O<sub>5</sub>-based (phosphate) systems. The first group comprises a wide range of glass formulations, including 45S5 Bioglass<sup>®</sup> and other typical compositions such as 1393 BG (wt%:  $53SiO_2$ - $6Na_2O$ - $12K_2O$ -5MgO-20CaO- $4P_2O_5$ ) [3] [4] [5] and S53P4 BG ( $53\%SiO_2$ - $23\%Na_2O$ -20%CaO- $4\%P_2O_5$ ) [6] [7] [8] commercially named as BonAlive<sup>®</sup> (BonAlive Biomaterials, Turku, Finland).

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