Bioactive Glass in Tissue Engineering: Progress and Challenges

Editorial

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Introduction

The quest for synthetic materials to be used in Tissue Engineering and especially in Bone Tissue Engineering, as expanded at a tremendous rate in the previous years. However, the challenging requirements to obtained scaffolds have led to difficulties in obtaining clinically relevant constructs. An optimum scaffold should be: 1) biodegradable, 2) osteoconductive or preferably osteoinductive, 3) porous (pore size >100 μm and porosity >70%), 4) manufactured in a reproducible manner and 5) mechanically stable. The great challenge in bone tissue engineering is to develop a material that will have a highly porous structure (with large pores) while having mechanical properties similar to the bone being restored. Since the discovery of the bioactive glass by L.L. Hench, this material, which exhibit not only osteoconductivity but also osteoinductivity, has attracted much interests in the field of bone tissue engineering but not only. Indeed, the typical silicate bioactive glasses demonstrated to bond to bone more efficiently than any other synthetic materials [1]. However, it was rapidly found that the highly disrupted silica network of bioactive glasses inhibits proper sintering at temperature below its crystallization [2]. Crystallization of bioactive glasses was found to decrease the rate of formation of the hydroxyapatite layer but does not completely suppress it [3]. Peitl et al. [4] demonstrated that even reduced, the bioactivity of a fully crystallized 45S5 bioactive glass remains higher than for pure A/W glass-ceramics [4]. Nonetheless, bioactive glasses were claimed to have great potential due to its ability to release ions beneficial for, but not limited to, wound healing, bone formation, and antimicrobial properties [5]. However, it is note that individual ion leaching is less predictable in fully or partially crystallized glasses as the ion release will depend on the crystal phase, content, dimensionality and more importantly to the composition of the remaining amorphous phase. Furthermore, the dissolution mechanism of the typical bioactive glasses, widely studied by Hench et al. [6] for the glass 45S5 and Andersson et al. [7] for the glass S53P4, is reported to be non-congruent. Such dissolution, leading to the formation of a thick SiO_2-rich layer, was found to lead to glass being left behind, unreacted, at the surgical site even 14-years post-surgery [8]. While silica-bioactive glasses products are having great success, such as BonAlive®, Bioglass®, Vitryxx®, just to cite a few, and in a wide range of clinical application ranging from cosmetics to bone regeneration, some of the drawbacks of the existing bioactive glasses should be overcome.

Recently much effort focused on new types of glasses such as bioactive phosphate, borophosphate and borosilicate glasses. These glasses are promising biomaterials and were found to be hot formed without significant crystallization. Work has been performed by Ahmed et al. [9] to demonstrate the potential of phosphate glasses as biodegradable and bioactive materials as well as their ability to be drawn into fibers for scaffolding materials [9,10]. Silver-phosphate, Iron-phosphate, titanium-phosphate and strontium-phosphate glasses, taken as example, demonstrated to show antimicrobial properties [11], cell attachment and proliferation as well as myotubes formation when using cell derived from H-2Kb-tsA58 immortomouse [12], similar gene transcription than Thermanox use as control [13] and similar gingival cell attachment and proliferation than typical bioactive glasses [14], respectively. An extensive review by Rahaman et al. [15] shows that borosilicate glasses have great potential in tissue engineering pertaining to their fast and more complete conversion into hydroxyl apatite than typical silica-based bioactive glass [15]. The main concern of borate containing glasses was the assume toxicity. This concern was alienated by studies on small animals [15].

Regardless of the bioactive glass composition studied various techniques have been employed to obtained scaffolds with large porosity, large pore size and mechanical properties for application in non-load bearing and load bearing applications. Many scaffolds have been developed that meet the requirements for non-load bearing application. Jones et al. for example developed scaffold with more than 80% of porosity and pore size from 100 to 500 μm using a sol-gel glass [16]. Scaffold obtained from polymer foam replication of various silica based bioactive glasses was successfully achieved by various authors [17-20]. Finally, solid free-form fabrication performed by Fu et al. [19] also show promising results [21]. Typically, thermal bonding of particles or fibers led to scaffolds with porosity lower than 70% [22-24]. As per load-bearing applications, no successful material was developed so far. The scaffolds developed by Baino et al. [25] as well as Huang et al. [26] taken as example, despite having mechanical properties similar to the cortical bone, possess porosity < 50% limiting their clinical potential [25,26]. However, it should be mentioned that in order to obtained a solid scaffold in all techniques tested, a

firing and sintering step is necessary. In most cases the sintering leads to scaffolds partially to fully crystallized. Furthermore, the use of bioactive glass and glass ceramics are also limited by their difficulties in handling due to their brittle nature.

Therefore, one of the challenge in tissue engineering is to develop bioactive glass scaffolds that can be processed with a controlled degradation and with a full conversion into a calcium phosphate reactive layer that will enable cell adhesion, proliferation and differentiation. The scaffold should have mechanical properties close to the tissue to be replaced while having porosity adequate for cell migration and angiogenesis. It is unlikely that one material alone will solve this engineering challenge. It is thus of paramount importance to develop new bioactive materials, that can fulfill the need for biodegradability, osteoconductivity, controlled degradation, and combine them with natural or synthetic polymers that will provide easier handling of the composite a well as elasticity and potential for drug delivery.

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