et al., 2016; Oruch et al., 2014; Forlenza et al., 2014; Chiu et al., 2013; Mertens et al., 2015). More recently, Zanni et al. (2017) found that Li^+ accumulates in neurogenic brain regions as revealed by high resolution ion imaging using time-of-flight secondary ion mass spectrometry.

It has also been demonstrated that Li^+ acts on the proliferation and differentiation of bone marrow mesenchymal stem cells, stimulating osteogenesis by activating different Wnt and Hedgehog (Hh) signaling pathways and inhibiting the enzyme glycogen synthase kinase-3β (GSK-3β) (Wu et al., 2014; Han et al., 2014; Wang et al., 2015; Geng et al., 2015; Thorfve et al., 2014a,b).

Recent experimental results have shown that Li^+ stimulates the in vitro secretion of growth factors with proangiogenic activity and participates in angiogenesis in vivo (Zeilbeck et al., 2014). It has also been shown that Li^+ induces the proliferation, migration, and survival of endothelial cells by activating the Wnt/β-catenin canonical pathway (Zeilbeck et al., 2014; Guo et al., 2009; Hedgepeth et al., 1997; Chen et al., 2000). These properties would constitute the rational base for the use of Li^+ in biomaterials feasible to be applied in regenerative medicine and in the engineering of tissues with a high degree of vascularization such as bone. Studies examining the effect of the addition of Li^+ into different biomaterials have mostly focused on the evaluation of the physicochemical and structural properties of these materials, while a few have considered the osteogenic potential of some of these materials (Wu et al., 2014; Han et al., 2014; Thorfve et al., 2014a,b; Fanovich et al., 1998; Wang et al., 2009; Khorami et al., 2011; Tylkowski and Brauer, 2013; Vilarinho et al., 2014; Brückner et al., 2016; Miguez-Pacheco et al., 2016; Gomillion et al., 2015; El-Kady et al., 2016; Li et al., 2017a; Vahabzadeh et al., 2017; Brauer et al., 2016; Khan et al., 2016; da Silva et al., 2017). In particular, the incorporation of Li^+ into BGs was first described by Khorami et al. (Khorami et al., 2011), who partially substituted Na_2O by variable amounts of Li_2O (3, 7, and 12 wt%) in a bioactive glass in the SiO_2-CaO-Na_2O-P_2O_5 (45S5) system. The results showed that the rate of formation of hydroxycarbonate apatite as an indicator of bioactivity was a dose-dependent phenomenon, which was delayed in glasses with a higher content of Li_2O (Khorami et al., 2011). These results are in agreement with recent findings of Bruckner et al. (Brückner et al., 2016) using 45S5 microparticles (<38 μm) with 6.1%–24.4% (mol%) of Li_2O, as well as with data reported by Miguez-Pacheco et al. (2016) for glass-ceramic scaffolds derived from the 45S5 bioactive glass with 2.5, 5, and 10 wt% of Li_2O, which showed that a content of up to 5 wt% of Li_2O maintains the bioactive behavior and thermal characteristics of the 45S5 bioactive glass.

It has been shown, both theoretically and experimentally, that the partial substitution of Na_2O for Li_2O on a molar basis in a 45S5 glass favors the compaction of the glass matrix because the smaller ionic radius of Li^+ (76 pm vs 102 pm of Na^+) and the greater tendency to form covalent Li-oxygen bonds cause the increase in oxygen density, defined as the concentration of oxygen atoms per volume unit of glass matrix (Brückner et al., 2016; Brauer et al., 2016; Brauer, 2015). The higher density of oxygen observed in glasses with Li_2O