contact with ionic dissolution products of BG60S glass (60% SiO_2) and biphasic calcium phosphate. BG60S releases silicic acid, which causes alkalinization due to the ion exchange process (Kaur et al., 2016c; Bosetti et al., 2003). Alkalinization enhances osteoblast/chondroblast proliferation because the calcium channels sensitivity increases enhancing calcium entry at the cellular level. BG60S dissolution products enhanced collagen production as compared to the BCP and control. Usually collagen I production is enhanced by silicic acid, whereas type I collagen RNA expression is stimulated by alkalosis (Bosetti et al., 2003; Reffitt et al., 2003). ALP production was similar among osteoblasts cultured on control, BCP, and BG60S. Osteoblasts were stimulated in higher calcium media to investigate whether calcium is responsible for the proliferation. Media with 100, 200, 300, and 500 mg/L of calcium were prepared. The cellular viability decreased after 300 mg/L, indicating that the calcium content is not related to the osteoblast proliferation. For MBG85 bioactive glass, SaoS-2 osteoblast proliferation is reduced in the presence of high Ca concentration (Alcaide et al., 2010), as well as phosphorous and calcium content upregulated Glvr-1 and Glvr-2 for murine adontoblast cells (Wittrant et al., 2009). Nrf 2 expression in osteoblastic cell (MC3T3-E1) increased upon treatment with 10 mmol phosphate (Beck et al., 2003).

Isaac et al. (2011) studied the effect of strontium doped bioactive glass on the osteoblast viability, proliferation, and differentiation. Two Sr-doped glasses, that is, B75-Sr1 (74 SiO_2-25.4 CaO-0.6 SrO) and B75-Sr5 (75.5 SiO_2-21.6 CaO-2.9 SrO), were used to study the bone cell behavior along with an undoped control B75 (73.7 SiO_2-26.3 CaO). Cell culture from fetal mouse calvaria closely mimics the cellular events of the intramembranous bone formation process; hence, it was used for cell cultivation. Collage-I was significantly higher in the presence of B75-Sr5 particles as compared with the presence of B75 and B75-Sr1 particles. Moreover, ALP mRNA also expressed more in the presence of B75-Sr5 after 6 days. BSP and osteocalcin were also expressed more in the presence of B75-Sr5 particles (Fig. 6.11). The gene profile for selected transcription factors like overall Runx2, Osterin, and Dix 5 showed almost similar profiles with mRNA levels significantly increasing up to day 12. The stimulation effect in the presence of B75-Sr5 particles is due to the strontium ions released from the bioactive glass particles into culture media. B75-Sr1 particles exhibited a limited effect on the osteoblast differentiation as compared to B75-Sr5. Hence, strontium ions enhanced bone cell replication and osteoblast differentiation as reported in studies (Canalis et al., 1996; Atkins et al., 2009; Peng et al., 2009). Sr containing 45S5 Bioglass depicted high biocompatibility without any inflammatory effects (Gorustovich et al., 2010b).

Asselin et al. (2004) investigated the behavior of chondrocytes isolated from the nasal septum cartilage of fetal rats cultured in 45S5 Bioglass and 60S glass (60 wt% SiO_2, less reactive). Matrix biomineralization is observed in the culture, which is in contact with 45S5 Bioglass. The levels of ALP