borate species (Ø representing an oxygen atom bridging two boron atoms) and silicate units (Lucacel et al., 2014). Luo et al. (Luo et al., 2010) reported that the addition of 0.75–2 wt% Ag to a borate bioactive glass did not affect the in vitro bioactivity of the glass upon immersion in an SBF. The formation of the HAP or HAP/AgCl layer on the glass surface can be limited or even stop the dissolution and release of silver ions. The released Ag ions in the AgBG surface layer can interact with phosphate and chloride ions (SBF), building silver phosphate compounds (e.g., Ag_3PO_4, $Ksp = 8.89 \times 10^{-17}$ at 25°C) and difficult soluble AgCl ($Ksp = 1.8 \times 10^{-10}$ at 25°C) (Houlsby et al., 1986). HAP biomaterials can incorporate silver ions into the structure during its formation, or they can be absorbed from the solution. Silver ions may have a strong stimulatory effect on the formation of carbonate apatite (Stanić et al., 2015). Boron-containing bioactive glasses with low silver content do not show cytotoxicity (Coelho et al., 2012; Miola et al., 2015; Luo et al., 2010; Xiao et al., 2012). Bioactive glasses doped with small amounts of silver ions showed a broad spectrum of antimicrobial activity (Magyari et al., 2014; Coelho et al., 2012; Miola et al., 2015; Luo et al., 2010; Xiao et al., 2012). Borate buffered solution also showed significant antimicrobial activity (Houlsby et al., 1986). Alkali borate glasses showed a bactericidal effect against Gram-negative bacteria (*Escherichia coli* and *Salmonella typhimurium*) and Gram-positive bacteria (*Staphylococcus aureus*) (Leipply et al., 2006). The Ag-doped borate bioactive glasses containing 0.75 and 1 wt% Ag were not toxic to the mouse MC3T3 osteoblasts and L929 fibroblast cells, whereas the glass containing 2 wt% Ag leads to a decrease in cell proliferation (Luo et al., 2010). An in vivo study showed that titanium implants coated with borate glass containing 1.0 wt% Ag_2O were most effective for simultaneously supporting fracture fixation and eradicating MRSA-induced infection within 6 weeks in a rabbit tibial model (Nezafati et al., 2012). Infection did not occur in animals with Ag-doped implants; in comparison, all 100% of the animals implanted with uncoated Ti and 70% implanted with bioglass-coated Ti (without Ag_2O) tested positive for the infection.

8.3.2 Copper-Doped Boron-Containing Bioactive Glass

Copper is an essential trace element to the structure of biomolecules and function of metabolism. It plays a physiologically important role in bone metabolism and wound healing. Several studies suggested that copper ions could enhance cell activity and proliferation of osteoblastic cells and inhibit osteoclast activity (Ewald et al., 2012; Zhang et al., 2003). Copper ions in vitro diminished the proliferation rate of mesenchymal stem cells but increased their ability to differentiate into osteogenic lineage (Rodríguez et al., 2002). They play a significant role in the process of angiogenesis and blood vessel maturation because they increase the expression of proangiogenic and growth factors (VEGF, bFGF, TNFα, and IL1β) and stimulate the human endothelial cell proliferation. Insufficient amounts of copper in a diet can cause anemia, neutropenia, and osteoporosis