

showed hierarchical macropores (300–500  $\mu\text{m}$ ) and ordered mesopores (5 nm), improved osteostimulation and angiogenesis ability, drug delivery, and antibacterial properties.

Bonici et al. (2012) developed bioactive sol-gel glasses in the ternary system  $\text{CaO-P}_2\text{O}_5\text{-SiO}_2$  doped with Cu. The oxidation state of Cu was optimized by tuning the process parameter in order to obtain nano-aggregates of metal nanoparticles into the glass matrix, glasses containing mixed  $\text{Cu}^{2+}\text{-Cu}^+\text{-Cu}^0$  nanoparticles, or  $\text{Cu}^{2+}$ -containing glasses. The antibacterial effect was not completely investigated, but the bioactivity was not affected by the presence of copper in the different oxidation states.

Among other metal ions, gallium and zinc have gained new interest in the scientific community, not only for their ability to enhance the bone-healing properties of bioactive glasses, but also for their antimicrobial properties (Valappil et al., 2008, 2009; Esteban-Tejeda et al., 2014, 2015). In particular, bioactive gallium-doped phosphate-based glasses have been recently shown to prevent *Pseudomonas aeruginosa* biofilms due to gallium ionic release (Valappil et al., 2008, 2009). New bactericidal coatings, based on biocompatible zinc-doped borosilicate antimicrobial glasses, have also been developed on different biomedical metallic substrates (titanium alloy, Nb, Ta, and stainless steel) (Esteban-Tejeda et al., 2014). By tailoring the glass compositions and the firing atmosphere, the thermal expansion mismatch with the substrate was adjusted, providing crack-free, single-layer coatings with strong antibacterial effect against *Escherichia coli*. The same authors developed a new family of low melting point borosilicate glasses with high ZnO content, which were chemically stable in distilled water, simulated seawater, Lysogeny broth (LB) and Dulbecco's modified Eagle medium (DMEM) media. These glasses have proven to be biocompatible showing, in addition, excellent biocide activity against Gram negative (*Escherichia coli*), Gram positive (*Staphylococcus aureus*), and yeast (*Candida krusei*).

## 2.4 PROMOTION OF ANGIOGENESIS

Angiogenesis, an important natural process used for healing and reproduction, is defined as the growth of blood vessels from the existing vasculature (Adair and Montani, 2010). Stimulation of angiogenesis can be used as a therapy to replenish blood supply in several conditions such as ischemic heart disease, wound healing, and peripheral arterial disease. Similarly, decreasing or inhibiting angiogenesis can be therapeutic in cancer treatments, ophthalmic problems, rheumatoid arthritis, and other common diseases (Adair and Montani, 2010).

The mechanism of angiogenesis allows the formation of new blood vessels from the preexisting ones and it is regulated by different factors, such as growth factors (e.g., vascular endothelial growth factor—VEGF), extracellular matrix proteins, cell membrane receptors, and other signaling molecules (Soker et al., 2000; Miguez-Pacheco et al., 2015).