observed when two or more ions are simultaneously applied (Wang et al., 2016; Stanic et al., 2010; Kalaivani et al., 2014; Ning et al., 2015). A study carried out by Wang et al. (2016) compared the bactericidal effects of Ag^{+}, Zn^{+}, and Cu^{2+} simultaneously and singly used against *Staphylococcus aureus*. The results showed that the ions had a synergetic effect when the three ions were combined.

14.1.2.2 Drug Release

There are different classes of antibiotics available for treatment of osteomyelitis, such as aminoglycosides, lipopeptides, glycopeptides, and lipoglycopeptides, among others (Straus and Hancock, 2006; Hickok and Shapiro, 2012; Sun et al., 2017; Popat et al., 2007; Wynn, 1985; Barbachyn and Ford, 2003; Nandi et al., 2009; Muraih et al., 2011; Kundu et al., 2012; Klinker and Borgert, 2015). Some of the most pertinent examples are described below.

Gentamicin is an example of an aminoglycoside. Its action mechanism is due to the inhibition of ribosome-related protein synthesis, which blocks the complexation of messenger RNA (mRNA). As a consequence, there is no synthesis of proteins, inducing bacteria death (Popat et al., 2007; Wynn, 1985).

Lipopeptides, like daptomicin, interact with the lipidic portion of the cellular membrane, forming aggregates at the inner part of the membrane, resulting in a disturbed structure, and causing bacteria death due to membrane depolarization (Straus and Hancock, 2006; Nandi et al., 2016; Muraih et al., 2011).

Vancomycin belongs to the glycopeptide class, being a drug commonly used in hospitals. Its mechanism is related to the inhibition of peptidoglycan synthesis, compromising the production of biomolecules that constitute the bacteria cell membrane (Hickok and Shapiro, 2012; Sun et al., 2017; Barbachyn and Ford, 2003; Klinker and Borgert, 2015; Yang et al., 2015). Careful administration of vancomycin is recommended, as there has been reported an increase in the MIC of vancomycin, mainly in the vancomycin-susceptible bacteria strains (Kaur et al., 2014). These data highlight a possible need of new antibiotics and new bioactive compounds as an alternative to the treatment of osteomyelitis.

Telavancin, olritavancin, dalbavancin, and teicoplanin are all examples of antibiotics belonging to the lipoglycopeptides class, being considered as comprehensive spectrum antibiotics; which means that the effect of these antibiotics covers both Gram-positive and Gram-negative strains. Therefore, these drugs could be used as an alternative to those currently applied in the treatment of osteomyelitis. However, their action mechanism is the same as that of vancomycin, which means that these drugs have to diffuse through the cell membrane. Owing to membrane diffusivity, the drug absorption kinetics is slow, and intravenous administration is required to overcome this challenge (Klinker and Borgert, 2015; Yenice et al., 2002).

Regarding the class of oxazolidine, drugs like linezoline and tedizolide show an action spectrum against a large number of Gram-positive strains (Barbachyn and Ford, 2003). In addition, they show a bioavailability of nearly 100% after