as well. It is expected that materials of high specific surface area can adsorb more drugs. The drugs adsorbed on the external surface, or inside large internal pores, tend to be preferentially released at the very beginning of body fluid contact, which is the cause of the burst effect. On the other hand, the drugs within smaller and deeper pores are responsible for the controlled release, because drugs at these pores are only released after the biomaterial is dissolved or degraded (Parent et al., 2017).

The drug release kinetics depends on the pore connectivity, because the more connected are the pores, the smaller is the course that the drug have to pass through before reaching the surface, and being released in the infected site. The drug absorption on the carrier surface depends on the chemical and physical interactions between them. It is considered as physical interactions: hydrogen bonds, hydrophobic interactions, van der Waals, and electrostatic forces. In contrast, are considered as chemical interactions the establishment of chemical bonds between the carrier and the drug. Usually, when a drug has chemical interactions with a carrier, the drug release kinetics is slower than when physical interactions are established instead (Parent et al., 2017).

The drug release can obey two main models: (1) Higuchi model, in which the drug diffuses through the pores of a carrier (Eq. 14.1); (2) Hixson-Crowell mode, in which the drug release occurs due to matrix erosion (Eq. 14.2). Both models of drug release can coexist in a drug delivery system, and the erosion (B) and diffusion (A) can be calculated by the Kopcha equation (Eq. 14.3) (Parent et al., 2017).

$$Q = a\sqrt{t} - b \tag{14.1}$$

where Q is the cumulative drug released; a is the release rate; b is the drug initial concentration; and t is the time.

$$\sqrt[3]{100} - \sqrt[3]{100 - Q} = ct \tag{14.2}$$

where Q is the cumulative drug released; c is the release rate; and t is the time.

$$Q = A\sqrt{t} + Bt \tag{14.3}$$

where Q is the cumulative drug released, A is the diffusion; B is the erosion, and t is the time.

Drug delivery systems are limited not only to delivery drugs, but also to delivery ions that have different therapeutic effects, such as osteogenesis and angiogenesis, and bactericidal activity. The simultaneous use of therapeutic ions and drugs can bring even more benefits to the treatment of bone infections associated with bone regeneration than when they are separately used (Wu and Chang, 2014).

14.1.2.1 Release of Ions

Considering that bacteria can resist antibiotics, an alternative to the treatment of bone infections is the use of metallic elements, which are known to have an antibacterial effect. Other advantages of ions with antibacterial effects include the comprehensive range of effect and low bacteria resistance. In addition, metallic