7 Sterile products packaging chemistry

Parenteral products are filled into primary packaging that is either glass or plastic. Many primary packaging systems, including vials, all bottles except for solutions for irrigation, syringes, and cartridges, are closed with some kind of rubber stopper, be it the closure on the vial or bottle or the septum and plunger for the syringe and cartridge. Irrigating solutions are packaged in glass bottles with screw caps rather than rubber closures. Products for topical application to the eye are packaged into plastic droptainers with plastic screw caps or, for ophthalmic ointments, into aluminum tubes and capped with plastic screw caps. Of course, all primary packaging is sterilized either prior to filling for aseptic processed products or terminally sterilized. This chapter focuses on some of the basic chemistry principles of glass (1–4), rubber (5–9), and plastic materials (10–12) and will highlight concerns about extractables and leachables from these surfaces (13–19). A review paper on which this chapter was based can also be a good source of information with additional references and coverage of convenient packaging delivery systems (20).

GLASS[1]

Glass is primarily composed of the element silicon. Silicon is a chemical element, one of the 109 known substances that constitute the universe's matter. Second only to carbon in its presence on earth, one-quarter of the earth's crust is silicon. Carbon is also the only element capable of producing more compounds than silicon.

However, one does not find silicon alone in nature. It always exists as silica or silicates. Silica is silicon dioxide (SiO_2), commonly found in sand and quartz. A silicate is a compound made of silicon, oxygen, and at least one metal, sometimes with hydrogen, sometimes without it. The most widely recognized synthetic form is sodium silicate, or water glass, a combination of silica with sodium and hydrogen. Materials lacking the molecular lattice structure of a solid state are amorphous, for example, all liquids. Thus, an amorphous form of a material possesses the same atomic makeup as the crystalline version, but without a highly ordered geometry.

The Assyrian King Ashurbanipal (669–626 BC) described glass as "Take 60 parts sand, 180 parts ashes of sea plants, 5 parts chalk–and you have glass" (21). Glass is an inorganic product of melting, which when cooled without crystallization, assumes a solid state. Glass is structurally similar to a liquid but has a viscosity so great at normal ambient temperatures that it is considered a solid.

Glass is employed as the container material of choice for most small-volume injectables. It is composed principally of silicon dioxide, with varying amounts of other oxides such as sodium, potassium, calcium, magnesium, aluminum, boron, and iron. The basic structural network of glass is formed by the silicon oxide tetrahedron. Boric oxide will enter into this structure, but most of the other oxides do not. The latter are only loosely bound, present in the network interstices, and are relatively free to migrate. These migratory oxides may be leached into a solution in contact with the glass, particularly during the increased reactivity of thermal sterilization. The leaching process is a diffusion controlled ion-exchange process involving exchange of hydrogen ions for the alkali ions present in the glass. The result is an increase in solution pH. This is especially problematic for packaged water products (e.g., Sterile Water for Injection) or dilute drug products that have little to no buffer capacity. Additionally, some glass compounds will be attacked by solutions and, in time, dislodge glass flakes into the solution. Such occurrences can be minimized by the proper selection of the glass composition and appropriate control of the container manufacturing process (discussed later).

[1] The technical information provided by Schott and Alcan are greatly appreciated.