A patented variation of the classical lyophilization technology is applied as VitriLife (3), wherein the product is lyophilized using a mixture of sugars; this formulation can be prepared in a much shorter time and is different from classic lyophilization in that no sublimation is involved and the product undergoes fast drying; the resultant product can be kept at room temperature, obviating the need for the cold chain for these products. The method has been applied to cholera vaccine and other vaccines and is still under development.

9.9.2.4.1 Stabilization through PEGylation

Where stabilization of native proteins is of great importance while in the formulation, the use of PEGylation is made to prolong the disposition half-lives of proteins in the body. It is a relatively new technique that requires fusing PEG molecule with the drug (Figure 9.15) and features the following:

- Improved bioavailability, including longer circulation time and slower clearance
- Optimized pharmacokinetics, resulting in sustained duration
- Improved safety profile, with lower toxicity, immunogenicity, and antigenicity
- Increased efficacy
- Decreased dosing frequency
- Improved drug solubility and stability
- Reduced proteolysis
- Controlled drug release

There are different types of PEGs. Linear PEGs are straight-chained PEGs that are monofunctional, homobifunctional, or heterobifunctional. Linear monofunctional PEGs (mPEG-X) have one reactive moiety at one end of the PEG, with the other end considered nonreactive (typically end-capped with a methoxy group). Linear homobifunctional PEGs (X-PEG-X) contain the same reactive moiety at each end of the PEG. Linear heterobifunctional PEGs (X-PEG-Y) contain a different reactive moiety at each end of the PEG. Branched PEGs (PEG2-X), also referred to as "Y-shaped" branched PEGs, contain two PEGs attached to a central core, from which extends a tethered reactive moiety. Forked PEGs (PEG-X2) contain a PEG whose one end has two or more tethered reactive moieties, extending from a central core. Multiarm PEGs (two-, three-, four-, and eight-arm PEG-Xs) are based on ethyoxylation of either glycerin (three-arm), pentaerythritol (four-arm), or hexaglycerin (eight-arm). The two-arm PEG was previously noted under the linear homobifunctional and heterobifunctional PEGs. Each arm has a tethered reactive group on the end. These multifunctional PEGs

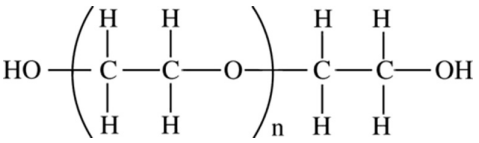

FIGURE 9.15 Structure of polyethylene glycol.