

methylcellulose, hydroxypropyl methylcellulose, and polyvinyl alcohol.

- *Vasoconstrictors and ocular decongestants:* Vasoconstrictors applied topically to the mucous membranes of the eye cause transient constriction of the conjunctival blood vessels. They are intended to soothe, refresh, and remove redness due to minor eye irritation. Among the vasoconstrictors used topically are naphazoline, oxymetazoline, and tetrahydrozoline hydrochlorides. Antihistamines, such as emedastine difumarate, ketotifen fumarate, and olopatadine hydrochloride, are included in some products to provide relief of itching due to pollen, ragweed, and animal dander.

PHARMACEUTICAL REQUIREMENTS

The preparation of solutions and suspensions for ophthalmic use requires special consideration with regard to sterility, preservation, isotonicity, buffering, viscosity, ocular bioavailability, and packaging.

Sterility and Preservation

Ophthalmic solutions and suspensions must be sterilized for safe use. Although it is preferable to sterilize ophthalmics in their final containers by autoclaving at 121°C (250°F) for 15 minutes, this method sometimes is precluded by thermal instability of the formulation. As an alternative, bacterial filters may be used. Although bacterial filters work with a high degree of efficiency, they are not as reliable as the autoclave. However, because final product testing is used to validate the absence of microbes, sterility may be ensured by either method. One advantage of filtration is the retention of *all* particulate matter (microbial, dust, fiber), the removal of which has substantial importance in the manufacture and use of ophthalmic solutions. Figures 17.1 and 17.2 show bacterial filtration equipment that may be used in the extemporaneous preparation of ophthalmic solutions.

To maintain sterility during use, antimicrobial preservatives generally are included in ophthalmic formulations; an exception is for preparations to be used during surgery or



FIGURE 17.1 Sterilization by filtration. The preparation of a sterile solution by passage through a syringe affixed with a microbial filter. (Courtesy of Millipore Corporation.)

in the treatment of traumatized eyes because some preservatives irritate the eye. These preservative-free preparations are packaged in single-use containers.

During preformulation studies, antimicrobial preservatives must demonstrate stability, chemical and physical compatibility with other formulation and packaging components, and effectiveness at the concentration employed. Among the antimicrobial preservatives used in ophthalmic solutions and suspensions and their effective concentrations are benzalkonium chloride, 0.004%



FIGURE 17.2 Examples of sterilizing filters. (Courtesy of Millipore Corporation.)