

Ethyl alcohol:	1.19 cP
Olive oil:	100.00 cP
Glycerin:	400.00 cP
Castor oil:	1,000.00 cP

Viscosity can be determined by any method that will measure the resistance to shear offered by the liquid. For ordinary Newtonian liquids, it is customary to determine the time required for a given sample of the liquid to flow at a regulated temperature through a small vertical capillary tube and to compare this time with that required to perform the same task by the reference liquid. Many capillary tube viscosimeters have been devised, and nearly all are modifications of the Ostwald type. With an apparatus such as this, the viscosity of a liquid may be determined by the following equation:

$$\frac{\eta_1}{\eta_2} = \frac{\rho_1 t_1}{\rho_2 t_2}$$

where

$\eta_1$  is the unknown viscosity of the liquid  
 $\eta_2$  is the viscosity of the standard  
 $\rho_1$  and  $\rho_2$  are the respective densities of the liquids, and  $t_1$  and  $t_2$  are the respective flow times in seconds.

In the preparation of ophthalmic solutions, a suitable grade of methylcellulose or other thickening agent is frequently added to increase the viscosity and thereby aid in maintaining the drug in contact with the tissues to enhance therapeutic effectiveness. Generally, methylcellulose of 4,000 cP is used in concentrations of 0.25% and the 25-cP type at 1% concentration. Hydroxypropyl methylcellulose and polyvinyl alcohol are also used as thickeners in ophthalmic solutions. Occasionally, a 1% solution of methylcellulose without medication is used as a tear replacement. Viscosity for ophthalmic solutions is considered optimal in the range of 15 to 25 cP.

## Ocular Bioavailability

Ocular bioavailability is an important factor in the effectiveness of an applied medication. Physiologic factors that can affect a drug's

ocular bioavailability include protein binding, drug metabolism, and lacrimal drainage. Protein-bound drugs are incapable of penetrating the corneal epithelium because of the size of the protein–drug complex (1). Because of the brief time an ophthalmic solution may remain in the eye, the protein binding of a drug substance can quickly negate its therapeutic value by rendering it unavailable for absorption. Normally, tears contain 0.6% to 2% of protein, including albumin and globulins, but disease states (e.g., uveitis) can raise these protein levels (1). Although ocular protein binding is reversible, tear turnover results in the loss of both bound and unbound drug (2).

As in the case with other biologic fluids, tears contain enzymes (e.g., lysozyme) capable of metabolic degradation of drug substances. However, only a limited amount of research has been conducted on the ocular metabolism of pharmacologic agents, so the full extent to which drug metabolism occurs and affects therapeutic effectiveness is undetermined (11).

In addition to physiologic factors affecting ocular bioavailability, other factors, such as the physicochemical characteristics of the drug substance and product formulation, are important. Because the cornea is a membrane barrier containing both lipophilic and hydrophilic layers, it is permeated most effectively by drug substances having both lipophilic and hydrophilic characteristics (1).

As discussed previously, ophthalmic suspensions, gels, and ointments mix with lacrimal fluids less readily than do low-viscosity solutions and so remain longer in the cul-de-sac, enhancing drug activity.

## Additional Considerations

Ophthalmic solutions must be sparkling clear and free of all particulate matter for comfort and safety. The formulation of an ophthalmic suspension may be undertaken when it is desired to prepare a product with extended corneal contact time, or it may be necessary when the medicinal agent is insoluble or unstable in an aqueous vehicle.

Drug particles in an ophthalmic suspension must be finely subdivided, usually