of time following instillation. Drug ionization is also important in determining drug solubility and permeability across the corneal epithelium. The extent of ionization can be manipulated through control of the pH of ophthalmic preparations.

Commonly used buffers in ophthalmic solutions include borate and phosphate buffers. To prepare solutions of lower pH range acetic acid/sodium acetate and citric acid/sodium citrate buffers are used. It is important that strong buffers are not used and to use a low concentrations of weak buffers.

Surface tension

The surface tension of tear fluid at physiological temperature in a healthy eye is 43.6 to 46.6 mN m^{-1}. Administration of solutions that have a surface tension much lower than that of the lacrimal fluid destabilizes the tear film and disperses the lipid layer into droplets that are solubilized by the drug or surfactants in the formulation. The oily film reduces the rate of evaporation of the underlying aqueous layer and therefore once it is lost, dry spots are formed which are painful and irritant. Surfactants are implicated in this.

Surfactants are typically included in ophthalmic preparations to solubilize or disperse drugs. Irritation power of surfactants decreases in the following order: cationic > anionic > zwitterionic > non-ionic. Non-ionic surfactants are therefore the most commonly used, examples include; polysorbate 20, polyoxyl 40 stearate, polyoxypropylene-polyoxyethylenediol. Despite being the least irritant, non-ionic surfactants have been shown to remove the mucus layer and disrupt the tight junctional complexes of the cornea; therefore increasing drug permeability. Surfactants may also interact with polymeric substances in the preparation and reduce the efficacy of preservatives. The concentration of surfactant is important not only in terms of drug solubility, safety and patient tolerance, but also because high concentrations can lead to foaming upon product manufacture or shaking.

Viscosity

Viscosity enhancing polymers are used in ophthalmic solutions to prolong drug retention in the precorneal tear film and thus enhance drug absorption. Mechanisms proposed are not just reduced drainage rate; the thickness of the precorneal tear film is also increased due to the ability of viscosity-enhancing polymers to drag water and stabilize the aqueous layer as they spread over the corneal surface on blinking. This increased volume acts as a reservoir for the drug so that it is re-spread in the tear film over the cornea with each blink. Water soluble polymers that have been used to increase solution viscosity include poly (vinyl alcohol), poly (vinylpyrrolidone), various cellulose derivatives, particularly; methylcellulose, hydroxypropyl methylcellulose and carboxymethyl cellulose (at concentrations of 0.2–2.5%) and poly(ethylene glycol)s (at concentrations of 0.2–1%).

Tears are non-Newtonian fluids whose coefficient of viscosity is shear dependent (shear-thinning). This is commonly seen with linear, multiple-charged polymers such as sodium hyaluronate and Carbopol. Zero shear viscosity values of 4.4 to 8.3 mPa s have been reported for normal tears. The force required by the eyelids to blink is 0.2 N and for a forceful blink it is 0.8 N. The pain threshold is 0.9 N and therefore if a higher force than this is required for blinking, then it would be painful for the patient. This limits the acceptable viscosity of administered ocular solutions since the force needed to move the instilled solution at the shear rates equivalent to those generated by blinking should be lower than 0.9 N. Furthermore, very viscous solutions can cause blurring of vision and may block the puncti and canaliculi. Nevertheless, solutions containing viscoelastic material can be used at higher viscosities. Since the viscosity of viscoelastic polymers is shear dependent; the viscosity of these polymer solutions can change in the eye due to blinking.

Topical, liquid ophthalmic preparations

Solutions

Ophthalmic solutions are the most common topical ophthalmic preparation. They are typically the easiest to manufacture (have the lowest cost of production) and are relatively easy for a patient or healthcare provider to administer. Ophthalmic solutions are also desirable where a rapid onset of action is required as they do not need to undergo dissolution. This would be the case for local anaesthetics (e.g. lignocaine, proxymetacaine hydrochloride); ocular diagnostics (fluorescein sodium) and ocular preoperative drugs. Moreover, solutions are homogeneous and therefore display a better dose