

Gels

Gels, which are semisolid systems comprising water-soluble bases, are also available and are more favourable than ointments for water soluble drugs. These utilize polymers such as polyvinyl alcohol (PVA), poloxamer, hydroxypropyl methylcellulose (HPMC), Carbopol or Carbomer, dispersed in a liquid. Pilocarpine is a cholinomimetic agent which reduces intraocular pressure and is licensed for glaucoma. It is available as a gel (Pilogel®, Alcon) containing more than 90% water and employing Carbopol 940 (a synthetic high molecular weight polymer of acrylic acid). An equivalent duration of response has been shown with a single instillation

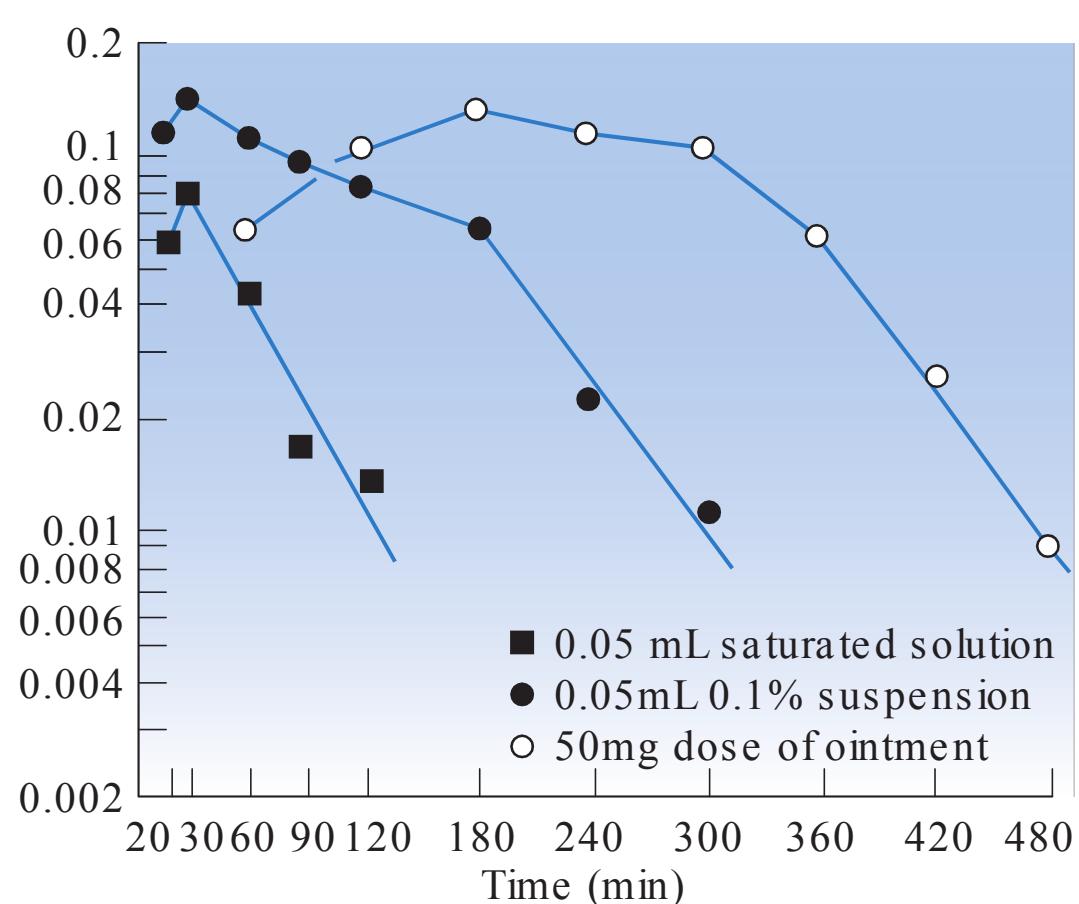


Fig. 41.3 • Comparison of aqueous humour levels of fluorometholone following administration by different dosage forms. (Courtesy of Sieg and Robinson, 1975, with permission.)

of the gel compared to four instillations of the solution. The total daily dose of pilocarpine can be reduced from 8 mg/day to 2 mg/day with the gel formulation.

Gels that are activated by ions, pH and temperature have also been developed. These undergo a phase transition from liquid to solid in the ocular cul-de-sac to form a viscoelastic gel. These *in situ* forming gels have an advantage over the pre-formed gels in that the dose is more reproducible and administration is easier; thus improving patient compliance. Examples of polymers activated by temperature include poloxamers e.g. poloxamer 407. Smart Hydrogel™ has been developed which is a graft co-polymer of polyacrylic acid and a poloxamer which requires only 1–3% polymer concentration to undergo gelation at body temperature. Smart Hydrogel™ also has bioadhesive properties due to the presence of polyacrylic acid.

Timolol is a non-selective beta blocker licensed for glaucoma. Timolol maleate gel-forming solution (Timoptic-XE®, Merck) is available in the clinic and constitutes a purified anionic heteropolysaccharide derived from gellan gum. The gellan gum is in aqueous solution and forms a gel in the presence of cations which are present in the precorneal tear film. It is administered once a day, compared to the regular Timoptic® preparation which needs to be administered twice daily to achieve a similar hypotensive effect. This gel is subsequently removed by the flow and drainage of tears. Alginates also undergo sol to gel phase transition when exposed to the ionic strength of ocular fluids. See Table 41.1 for examples of gel and gel-forming ophthalmic preparations.

Table 41.1 Examples of gel and gel-forming topical ophthalmic preparations

Active ingredient	Brand name and dosage form	Therapeutic class and indication	Release controlling excipient
Timolol maleate	Timoptol LA/Timoptic XE (gel forming solution)	Beta-blocker for glaucoma. To be applied once daily.	Gellan gum
Betaxolol	Betoptic S (eye drops)	Beta-blocker for glaucoma. To be applied twice daily.	Amberlite® IRP-69 (cationic exchange resin)
Levobunolol hydrochloride	Betagan (eye drops)	Beta-blocker for glaucoma. To be applied once or twice daily.	Polyvinyl alcohol
Pilocarpine	Pilogel (gel)	Miotic. To be applied once daily at night.	Carbomer 940
Fusidic acid	Fucithalmic (eye drops)	Antibacterial. To be applied twice daily.	Carbomer