slapping water with the hand. Also, even solid materials would flow if a high enough stress was applied for a sufficiently long time.

The application of rheology in pharmaceutical formulation

The components used to make a formulation may not only affect the physical and release characteristics of the product but may also guide it to the site of absorption. In some cases it may be possible to exploit the properties of the excipients such that the dosage form is retained at a specific location in the body. This approach is often necessary for locally acting products which are used to treat or prevent diseases of, for example, the eye and the skin. To treat conditions in the eye an aqueous solution of the drug is delivered to the precorneal area by means of a dropper. If the solution is Newtonian and of low viscosity, then it will be rapidly cleared form the eye as a result of reflex tear production and blinking. The resultant short residence time means that an effective concentration will only be attained for brief periods following dosing so that treatment is pulsatile. However, if a water-soluble polymer is added to the formulation, such that the viscosity is within the range of 15–30 mPas, then the residence time increases as does the bioavailability. Addition of excipients that make the product pseudoplastic will facilitate blinking and this may improve acceptance and compliance by the patient. If the product can be made viscoelastic then solutions of higher consistency may be tolerated. This can be achieved in the eye if a polymeric solution is designed to be Newtonian when it is instilled, but then undergoes a sol-gel transition *in situ* in reaction to the change in environment such as temperature, pH or ion content. Polyvinyl alcohol, cellulose ethers and esters and sodium alginate are all examples of polymers which have been used as *viscolysers* in eye drops. Polyacrylic acid and cellulose acetate phthalate have been claimed to produce reactive systems. The formulation of eye drops and the importance of viscosity in formulation of ocular delivery systems are discussed further in Chapter 41.

The ointments and creams which are applied to the skin to deliver a drug which has a local action, such as a corticosteroid or anti-infective agent, are usually semi-solids. Their rheological properties need to be assessed after manufacture and during the shelf-life in order to ensure that the product is physically stable; this is important because the rate of release of the drug and the concentration at the site of action is related to the apparent viscosity. Since these products are packaged in flexible tubes then rheological measurements will also indicate whether the product can be readily removed from the container (see also Chapter 39).

Knowledge of the flow properties of a product such as a gel for topical application can be used to predict patient acceptability, since humans can detect small changes in viscosity during activities such as rubbing an ointment on the skin, shaking ketchup from a bottle or squeezing toothpaste from a tube. Since the ability of the body to act as a rheometer involves the unconscious coordination of a number of senses, the term *psychorheology* has been adopted by workers in this field. All three situations provide examples of the advantages of designing a formulation which has a yield stress and exhibits plastic or pseudoplastic behaviour so that the patient only has to apply the appropriate shear rate.

Transdermal delivery systems (often referred to as *patches*) are used to deliver drug across the skin at a rate which means that they can be left on the skin for periods of up to a week. The drug can either be incorporated in a reservoir or dissolved in the layer of adhesive which holds the device on the skin (Chapter 39). The rheological properties of the adhesive can therefore be used to predict and control not only the adhesion but also the rate of absorption of the drug. The latter can be used to estimate the length of time that device needs to be applied to the skin.

When a dosage form is intended to be administered perorally, so that the active ingredient can be absorbed from the gastrointestinal tract, then the gastrointestinal transit time plays a major role in the extent and amount of drug which appears in the blood stream. The first phase of gastrointestinal transit is gastric emptying, which is in part dictated by the rise in viscosity of stomach contents in the presence of food. The consequential increase in gastric residence time and fall in the dissolution rate of the active ingredient can lead to a reduction in the rate, but not necessarily the extent, of absorption. Such effects can be exploited by the pharmaceutical formulator, for example, by including a gel-forming polymer in the formulation, since this can simulate *in vivo* the effect exerted by food. However, its use as a means of prolonging the duration of action of an orally administered medicine