

$$\eta = \eta_k \rho \quad (9.8)$$

where  $\rho$  is the density of the solution in  $\text{g/cm}^3$ .

### ***Falling ball viscometer***

This type of viscometer is used for measuring Newtonian fluids. In the falling ball viscometer, a spherical steel ball is allowed to fall through a tube containing the solution to be measured. Yuan and Lin have reviewed this method, which is seldom used for determination of viscosities of proteins (Yuan & Lin, 2008, p. 40) since the measurements are complicated by the necessity of using up to six balls to span the viscosity range. However, Patapoff and Esue used a falling ball viscometer to determine bulk viscosity of a mAb solution as a function of polysorbate 20 addition (Patapoff & Esue, 2009). They showed a slight, but negligible increase in viscosity with addition of polysorbate 20.

### ***Rotational rheometers***

The most common method used to determine viscosities of protein solutions is the rotational rheometer. Rheometry extends the determination of viscosity to also investigate the elastic properties of solutions, which are a determination of how energy is stored during the flow and deformation of the fluid. These rheometers investigate a fluid that is sheared between a static and rotating surface. There are several geometries used including parallel plates, concentric circles, and one of the most used geometries, a cone and plate. In this rheometer, the lower circular plate is flat and the upper plate is a truncated conical plate with a common cone angle of  $1\text{--}3^\circ$ . Removal of the apex of the cone that intersects the lower plate allows for precise determinations of a uniform shear rate resulting in a shear stress,  $\sigma$ , that is related the applied torque,  $M$  (Newtons meter) and the cone radius,  $R$  (m):

$$\sigma = 3M/2\pi R^3 \quad (9.9)$$

Then the viscosity,  $\eta$ , is related to  $M$ ,  $R$ , the angular velocity in radians/s,  $\omega$  and the cone angle in radians,  $\alpha$ :

$$\eta = 3M\alpha/2\pi R^3 \omega \quad (9.10)$$

Another type of a rotational rheometer is one that uses parallel plates, and is often used for characterization of elasticity by observing the properties of fluids placed between the two oscillating plates. The main advantage of this method is that with a small gap between plates the volume required for a measurement is greatly reduced, and that very high shear rates can be achieved with the smaller gap size. Some of the problems that can occur with this method, such as errors in gap size for small gaps, are summarized by Jezek et al. (2011).

It has been reported that using a cone and plate rheometer resulted in extensive shear thinning for an IgG<sub>1</sub> mAb whereby after multiple shear cycles viscosity increased due