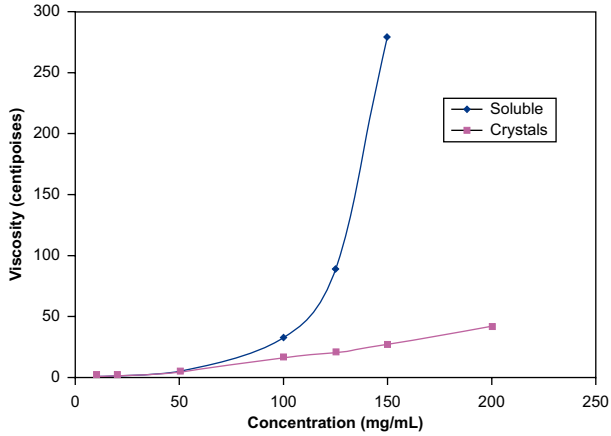

Figure 7.7 Viscosity measurements of infliximab. Infliximab (100 mg/vial containing 500 mg of sucrose, 0.5 mg of polysorbate 80, 2.2 mg of monobasic sodium phosphate (monohydrate), and 6.1 mg of dibasic sodium phosphate (dihydrate)) was reconstituted in water to concentrations of 10, 25, 50, 100, 125, and 150 mg/mL and compared with various concentrations of crystalline suspensions. For crystalline suspensions of infliximab, a 200 mg/mL solution (which was in formulation buffer containing 10% ethanol, 10% PEG 3350, 0.1% Tween 80, and 50 mM trehalose in 50 mM sodium phosphate buffer, pH 7.0) was tested for viscosity in addition to the concentrations mentioned above for soluble infliximab.
Reproduced from Yang et al. (2003).

Using formulation excipients to reduce viscosity

As discussed, formulation development is important in designs of new manufacturing processes. Much of the alternate process development used lyophilization and spray drying, which require appropriate excipients to stabilize the protein/mAb from the stresses that occur during the alternative drying processing. On another tact, it would be highly desirable to create a liquid formulation that can be easily manufactured using TFF. High viscosity at high concentrations is clearly one of the challenges that need to be overcome, and thus it is imperative to use excipients that can lower viscosity in a liquid formulation. In later chapters the role of PPI will be discussed, particularly attractive interactions, which appear to be a major contributor to the high viscosities that have been observed for some mAbs. The nature of these interactions will dictate what excipients are most effective in disrupting these interactions. In early studies by Liu et al. (Liu, Nguyen, Andya, & Shire, 2005) it was shown that attractive electrostatic interactions predominate at the high concentration of an IgG_1 mAb, and that addition of NaCl was effective in lowering viscosity (this will be discussed in more detail in Chapter 9). In subsequent studies by Kanai et al., it was shown that addition of cations appears to reduce the viscosity of this mAb by screening of interactions whereas binding of anions to the mAb is involved in the viscosity reduction (Kanai, Liu,