sparingly soluble crystalline hydrate, and that the raw material was an amorphous (much more soluble) form of the drug. Seeds, and unfortuitous ratios of alpha and beta epimers of the calcium gluceptate, catalyzed the precipitation.

Precipitation is a nucleation and crystal growth phenomenon (Carstensen and Rodriguez, 1985, Rodriguez, Hornedo and Carstensen, 1985), and as such it can be impaired or prevented by inhibitors. These are often viscosity-impairing substances (carboxymethyl cellulose for instance), and hence the stability of the viscous component becomes important. The loss of this can be detected by following viscosity.

The viscosity of these agents is often Bingham bodies, i.e., they possess a yield value. The correct way of checking them is, therefore, with e.g. a cup-and-bob viscometer, so that a rheogram can be drawn. In this fashion it is possible to check both changes in yield value and slope of the rheogram (apparent viscosity). For very fluid solutions (dilute aqueous solutions) this is difficult, and most often it is best followed by the use of an Ostwald–Fenske pipette. Two pipettes (with different flow times) should be used in this case, because the difference in the measured viscosity is a measure of the yield value (although calculation of the yield value from the difference is a priori not possible). Both yield value and apparent viscosity are functions of concentration (Ben-Kerrour et al., 1980); in a multicomponent system there will usually be one main component responsible for viscosity, and it is the breakdown of this one compound that would be of importance. Often when drastic changes occur in viscosity, bacterial contamination can be suspected.

Precipitation is tied into solubility, as seen in the foregoing. Solubility can be augmented by various means. In the case of cloud times, the use of cosolvents (e.g., polyethylene glycol) will increase the value of S. Other methods are the use of a micellar approach and the use of complexation. A recent example of this latter is the work by Mehdizadeh and Grant (1984) on the complexation behavior of griseofulvin with fatty acids. Order of magnitude increases in solubility were reported.

2.4 Oral Solutions

The main types of changes in appearance of oral solutions (syrups, elixirs, etc.) are loss of dye, precipitation, and bacterial growth. Precipitation has already been dealt with to some degree, but some cases particular to oral solutions will be mentioned. Change in dye content will be treated below. Bacterial growth will be treated separately.

Scott et al. (1960) showed the loss of blue dye in a vitamin syrup, and showed that it could be treated exactly like a drug substance. Predictions by Arrhenius plotting are quite good in the case of degradation in solution, because the homogeneity is good. Figure 2 shows an example of this.

3. DISPERSE SYSTEMS

Disperse systems are suspensions and emulsions. The rationale for the physical tests carried out on these will be discussed below.