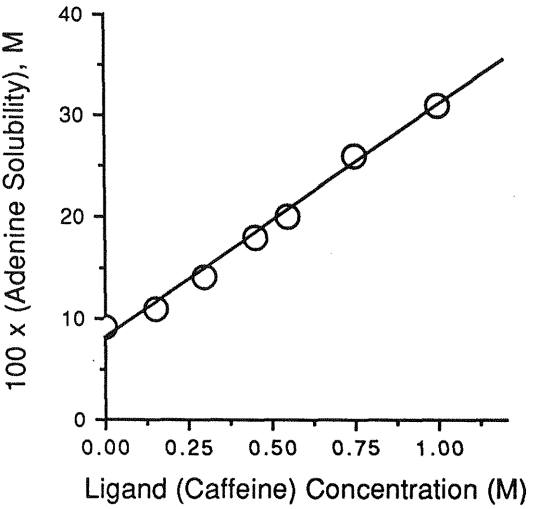

Fig. 3 Least squares fit: $y = 0.26x + 0.0076$, where x is solubility (rather than $100 \times$ solubility, as used in the figure). (Graph constructed from data published by Chen et al., 1994.)

plexes are those with cyclodextrins: for instance Connors and coworkers have published substantially in this area (Pendergast and Connors, 1984; Connors et al., 1982). Duchene et al. (1986) have reviewed the effect of cyclodextrin complexes on drug stability. Lach and Chin (1964a) have studied the complexes of cyclodextrins with benzocaine and found them to be 1 : 1 complexes. Higuchi and Lachman showed that benzocaine complexed with caffeine (1955). Lach and Chin (1964b) showed that a series of substituted benzoic acids complexed with cyclodextrin. Cyclodextrins are unique (alpha, beta, and gamma) in that they are doughnut shaped molecules that allow inclusion of the drug molecule. Other (non-macrocyclic) carbohydrate molecules also complex, for instance Gupta (1983) has shown that procainamide complexes with glucose, lactose, and maltose. All of these have a hemiacetal group, as opposed to sucrose and fructose. The complex formation was pH dependent.

Complexation constants may be obtained by spectrophotometric means as well. The complex can exhibit a specific maximum in the ultraviolet spectral range, so its concentration can be distinguished from that of the parent species such as in the case of the alendronate/Cu^{++} complex and the case of metal complexes of anhydrotetracycline (Siqueira et al., 1994).

2.1. Complexing Agents

Caffeine and polyvinylpyrrolidone were the most common complexing agents used in pharmaceutics for a series of years. In recent years the cyclodextrins have become of importance.

An example of this is the work by Van Der Houwen et al. (1994) dealing with the kinetics of 7-*N*-(*p*-hydroxyphenyl)mitomycin C (M-83) in the presence of γ-cyclodextrin. The pH profile of this is V shaped with a couple of extensions of