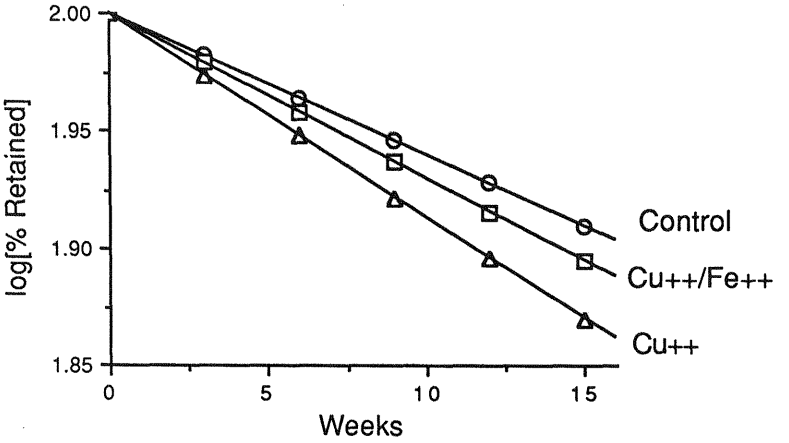

Fig. 1 Effect of metal ions on the decomposition of ascorbic acid. Least squares fit lines are (Control) $y = 2 - 0.006x$, (with copper and iron) $y = 2 - 0.007x$, (with copper alone) $y = 2 - 0.0087x$. (Figure constructed from data published by Kassem, 1969.)

in aqueous solutions. They are 1 : 1 complexes with relatively high stability constants. Upadrashta and Wurster (1988) used ethylene diamine tetraacetic acid to protect anthralin solutions from metal catalyzed oxidation. Tomida et al. (1987) showed that zinc ion increased the degradation of cephalosporins in tromethamine solution. The second-order rate constant, divided by $[Zn_o]$ plotted versus pH has unity slope from pH 7.5 to 8.5. They suggest the formation of a ternary complex (penicillin-Zn^{2+}-tromethamine).

Substances such as vitamin A and D are also prone to metal ion catalyzed decomposition.

Of other works in this area, McCrossin et al. (1998) reported on the effect of guanidine HCl on degradation of recombinant porcine growth hormone at alkaline pH and different concentrations and found it to be first order.

Fredholt et al. (1999) studied the catalytic effect of α-chymotrypsin on desmopressin decomposition and reported on the influence of concentration, pH, and cyclodextrin. The reaction is presumably A-B-C and the disappearance rate of the compound is first order. The pH profile is type AHJD with a maximum at pH 7.7.

2. COMPLEXATION

It is obvious that in many cases, drugs may complex with one or more of the ingredients in a solution dosage form. Sometimes this is intentional, e.g. bioavailability in certain instances may be improved (Levy and Reuning, 1964; Newmark et al., 1970). In other instances the stability of a drug is favorably affected by complexation, although in many cases the opposite is the case.

The basic principles of complex formation have been reviewed by Connors and Mollica (1964) and demonstrated by them as well. Only the formation and stability of 1 : 1 complexes will be covered here. For coverage of 1 : 2 and 2 : 1 complexes,