3. TYPES OF SURFACE MOISTURE

There are, broadly speaking, three types of situations: *Limited water*, where all the water is used up in the decomposition of the drug, but the amount is not enough to decompose all of the drug.

Adequate water, when there is enough moisture to decompose all of the drug substance.

Excess water, when the amount of water present is more than needed to dissolve the drug completely.

3.1. Excess Water

This is shown as E in Fig. 1, where the amount of water suffices to bring all of the drug into solution. This may not be applicable initially, but it occurs as the amount of parent drug decreases in time.

Examples of this are the work by Morris (1990), where the indomethacin/water system was studied in a closed system at 130°C. After a short period of time a eutectic consisting of indomethacin, decomposition products, and water is formed, and from this point in time the decomposition is first order as expected for solution kinetics (Fig. 2). The amount of time (t') required for the eutectic to form (for the mass to form a homogeneous liquid) is linear in water activity ($a = \mathrm{RH}/100$), i.e.,

$$t' = \beta - q'a \tag{7.9}$$

where β and q' are constants (Fig. 3).

Yoshioka and Uchiyama (1986a,b), Carstensen et al. (1987), and Yoshioka and Carstensen (1990a,b) have reported similarly in relationship to propantheline bromide. Yoshioka and Uchiyama (1986a) introduced *critical relative humidity* (CRH) as the point where the water activity just equals that of a solution saturated

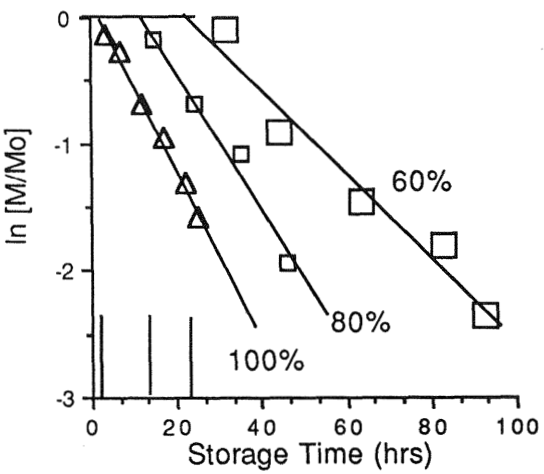

Fig. 2 Decomposition of indomethacin in the presence of moisture at 130°C. (Graphs constructed from data published by Morris, 1990.)