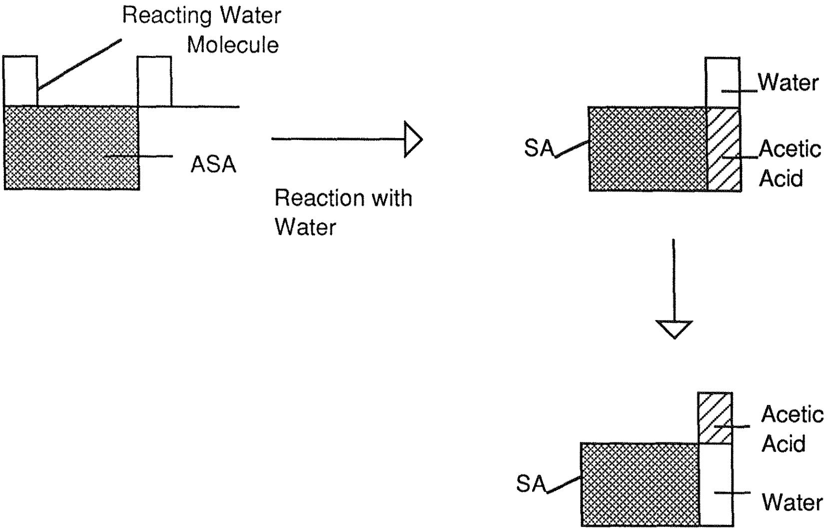

Fig. 11 Surface active site interaction using aspirin as an example. (Graph constructed from model proposed by Attarchi, 1984, and Attarchi and Carstensen, 1988.)

The amount of water does not suffice to "dissolve" the active sites, so the reaction is an interaction between moisture and drug at the activated site. The development of such a model has been published by Attarchi (1984) and Carstensen and Attarchi (1988). The applicable equation is Eq. (7.9):

$$\ln\left[\frac{x}{1-x}\right] = k(t - t_{1/2}) \tag{7.14}$$

The applicable model is presented in Fig. 11. Data plotted in this fashion is shown in Fig. 11, and the rate constants admirably follow an Arrhenius equation as shown in Fig. 12.

Obtaining the actual values of k and S in Eq. (7.2) is not as easy as might seem. As pointed out (and investigated) by Attarchi (1984) and by Carstensen and Attarchi (1988), both k and S are a function of amount of decomposition product. This was first pointed out by Pothisiri (1974), by Pothisiri and Carstensen (1975), and by Wright and Carstensen (1986). It is also a function of ionic strength, as pointed out by Gerhardt (1990) and by Gerhardt and Carstensen (1989), or simply a function of the composition of the sorbed moisture layer (Attarchi, 1984; Carstensen and Attarchi, 1988; Pothisiri, 1974).

8. DOSAGE LEVEL AND TOXICITY CONSIDERATIONS

In a great majority of cases the decomposition is zero order i.e., following Eq. (7.5). This means that the amount of decomposition product is linear in time.

If a product, for instance, is made in three dosage strengths, say 5 and 25 and 50 mg strengths, then after 3 years' storage at 25°C an amount of e.g. 0.075 mg has been decomposed, i.e., (assuming for simplicity equal molecular weights) 0.075 mg of decomposition product has formed (see Fig. 13). Since Eq. (7.5) is a