suffer from being *one point data*, so dissolution/disintegration correlations cannot be deduced from the reported figures.

8.8. Dissolution Media

There is always the problem of what dissolution medium to use. For poorly soluble drugs there are several approaches: cosolvents, micellar systems, and/or large dissolution volumes. Naylor et al. (1993) studied the mechanism of dissolution of hydrocortisone in simple and mixed micelle systems by using a rotating disk and found the Levich equation to hold.

8.9. In-Vivo to In-Vitro Correlation

The problem of whether an in-vitro dissolution test generally measures in-vivo performance on a rank scale basis is still open to debate, when the problem is considered in general, i.e., if product A from manufacturer A has a dissolution rate curve "above" that of manufacturer B, will his product also have a better in-vivo performance as far as large magnitude (C_{max}) and short peak time (T_{max}) for the maximum of the blood level curve and high value for the area under the blood level curve (AUC)? The general premise is that the answer is yes, but as shall be seen below, this is not necessarily so. The correct general statement is that if two batches of the same product and formula are tested, then such a comparison is correct, i.e., that a "higher" dissolution curve implies at least one of the following: lower T_{max}, higher C_{max}, or higher AUC. An example of noncorrelation, when the formula is not the same, is the work by McNamara et al. (1987), in which furosemide from five manufacturers was tested against a solution. The relative rankings are shown in Table 5.

It is seen, then, that the best performer in vivo (D) is by no means the best performer in vitro, and that the worst performer in vitro (E) is not the worst performer in vivo.

The best and simplest method for correlation of in-vitro to in-vivo data would appear to be the mean residence time (MRT), and such comparisons have recently been described by Block and Banakar (1988). MRT is defined by many authors as shown in Fig. 26. The MRT factual definition is a measure of the "average" length of time a drug molecule is in the body (Fig. 26).

Mean residence time via statistical moment has also been described by Yamaoka et al. (1978). Podzeck (1993) has compared in-vitro dissolution profiles by calculating mean dissolution time and mean residence time.

Of late, deconvolution has been often reported and may form part of the 1995 USP. This method consists of comparing a blood level curve after solid dosage form administration with one after either solution or IV administration. The amount dissolved in the GI tract is then obtained by deconvolution. Sugawara et al. (1994) tested a series of controlled release preparations of prednisolone in alginate gel beads, all in a drug-to-alginate ratio of 1:4. As seen in Fig. 27, they were able to obtain in-vitro methods that "matched" the amount released in-vivo.

It is seen in the figure that for the fast releasing formulation (a), the in-vitro test, whether at pH 1.2 or at pH 6.8, follows the deconvoluted in-vivo results fairly well, but for the slow formula, it is only the pH 1.2 in-vitro test that correlates with the deconvoluted in-vivo dissolution test.