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The concept of dissolution efficiency

The recent interest in drug availability has resulted in a proliferation of *in vitro* dissolution testing, now standard for many dosage forms. The usual method of evaluation is the comparison of the time taken for given proportions of the active drug to be released into solution and figures such as the $^{t}20$, $^{t}50$ and $^{t}90\%$ times are often quoted. Alternatively the fraction of drug in solution after a given time is used for comparison, i.e. 60% release in 30 min.

A further parameter suitable for the evaluation of *in vitro* dissolution has been suggested by Khan & Rhodes (1972), who introduced the idea of Dissolution Efficiency. This is defined as the area under the dissolution curve up to a certain time, t, expressed as a percentage of the area of the rectangle described by 100% dissolution in the same time. The simplest case, dissolution of a tableted drug, is shown in Fig. 1 where,

$$\text{Dissolution Efficiency (D.E.)} = \frac{\int_0^t y.dt}{y_{100}.t} \cdot 100\%$$

Before mentioning the advantages of this concept, the following points should be appreciated:

1. The Dissolution Efficiency can have a range of values depending on the time intervals chosen. This should preferably be greater than the $^{t}90\%$ of the formulation to ensure that most of the dissolution pattern is taken into account, although this is not always convenient with slowly released drugs. In any case, constant time intervals should be chosen for comparison. For example the index $D.E.^{30}$ would relate to the dissolution of drug from a particular formulation after 30 min and could only be compared with the $D.E.^{30}$ of other formulations.

2. With formulations in capsules, there are two schools of thought on whether or not the lag time should be included in the calculation (Fig. 2). If a comparison of various capsule fills is desired then assuming there is no interaction between capsule contents and gelatin shell, the lag time could be excluded as in (a) Fig. 2. However, if a final product is being tested, i.e. production or storage test samples, the lag time would be included as in (b) Fig. 2.

3. It is essential to establish that the total content of drug in the formulation is available for release and is not insolubilized by interaction with, or adsorption by, formulation aids. This is also the case with other methods of treating *in vitro* dissolution results.

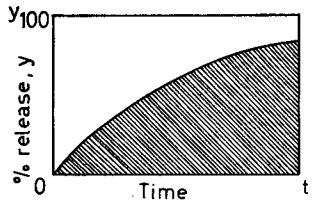

FIG. 1. Dissolution of drug from a tablet:

$$\text{D.E. (\%)} = \frac{\text{shaded area}}{\text{rectangle } y_{100}\ ^{t}} \times 100$$

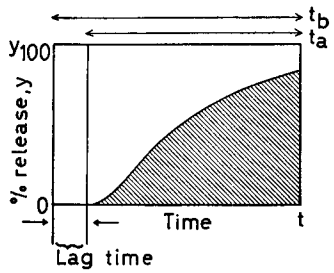

FIG. 2. Dissolution of drug from a capsule.

^{t}a Time interval chosen begins with release of drug:

$$\text{D.E. (\%)} = \frac{\text{shaded area}}{\text{rectangle } y_{100}\ ^{ta}} \times 100$$

^{t}b Time interval measured from time of capsule insert:

$$\text{D.E. (\%)} = \frac{\text{shaded area}}{\text{rectangle } y_{100}\ ^{tb}} \times 100$$

4. Dissolution Efficiency is a comparative parameter and should be quoted in conjunction with the $^{t}50\%$ or preferably $^{t}90\%$ value.

The concept of Dissolution Efficiency has certain advantages. The first is that summation of drug release data into a single figure enables a ready comparison to be made between a large number of formulations. The second advantage, and probably the most important, is that it can be theoretically related to *in vivo* data. If it is assumed that the degree of absorption of a drug *in vivo* is proportional to the concentration of the drug in solution and the time this solution is in contact with a suitable absorptive region of the gastrointestinal tract, it can be seen that the Dissolution Efficiency as described is a function of these two variables. It therefore appears logical that since *in vivo* drug availability is estimated by integrating the area under the blood level curve it seems reasonable to express *in vitro* results similarly. Also, when a relation is to be shown between dissolution and another variable (e.g. the effect of tablet compaction pressure), it is perhaps more realistic to use Dissolution Efficiency which takes into account the dissolution profile as a whole, as opposed to $^{t}50$ or $^{t}90\%$ values which use just one point from the plot. Furthermore, it is possible that the relation shown to exist between a formulation factor and $^{t}50\%$, may not apply to $^{t}20\%$ or $^{t}90\%$ times.

Various methods of measuring the area under the dissolution curve have been tried, e.g. counting squares, using a planimeter, cutting-out and weighing, etc. and the latter method has been found most accurate, reproducible and convenient.

The author is grateful to Mr. G. Wade for useful discussions and for his help in evaluating the concept in experimental work.

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July 19, 1974

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