A PROPOSED COMBINED DISSOLUTION AND STABILITY TABLET TEST

R.B. Taylor, A.B. Selkirk and K. Purrell, School of Pharmacy, Robert Gordon's Institute of Technology, Schoolhill, Aberdeen, AB9 1FR, U.K.

An intrinsic tablet dissolution test when carried out by an adequately specific analytical procedure depends for its validity on the active ingredient being chemically stable in solution during the dissolution test. It is possible by analysing the resultant solution for both active ingredient and decomposition product to verify the accuracy of the dissolution test with respect to possible decomposition and to estimate the rate constant for the decomposition.

Aspirin, 500 mg, was tabletted at 350 MNm^{-2} and the resultant tablet coated with epoxy resin on all but one face. The coated tablet was mounted on a shaft connected to a constant speed motor and rotated in solutions of controlled pH to provide an approximation to the rotating disc method of Wood et al (1965). During dissolution the solution was assayed for aspirin and salicylic acid at various times by hplc and the results were plotted for different pH and stirring rates. The apparent zero order dissolution rate constants (k_o) were estimated as the initial slope of the aspirin line. The first order rate constants (k_1) for the decomposition were estimated from the slope of the line obtained by plotting the gradient of the salicylic acid-time curve at various times against the corresponding aspirin concentration. This approach using modern analytical methods has the putative advantage that low decomposition rates may be determined within a short experimental time scale as a consequence of the high sensitivity available in favourable cases. The results shown in Table 1 indicate good agreement between literature and experimental values of k_1.

Table 1. Derived Constant from Combined Dissolution Stability Test

pH	Stirring rate (r.p.m.)	$k_o \times 10^2$ (mg $h^{-1}cm^{-2}$)	$k_1 \times 10^5$ (min^{-1})	Literature $k_1 \times 10^5$ (min^{-1})
1.3	100	2.0	107	24
2.5	100	2.7	7.1	3.7
10	100	3.4	185	150
2.5	50	1.4	4.8	3.8
2.5	130	2.9	6.6	3.8
2.5	200	3.6	5.0	3.8

The importance of monitoring decomposition simultaneously with dissolution will increase with increasing instability of the active ingredient. In the situation where the dissolution rate is markedly altered by the decomposition process, the scheme

$$\text{Tablet} \longrightarrow \text{Drug } [D] \longrightarrow \text{Product, yields kinetically } [D] = \frac{k_o}{k_1}(1 - e^{-k_1 t})$$

If k_o is established by the method described above at low concentrations, the value of k_1 can be obtained by an iterative curve fitting program using the remaining parts of the experimentally obtained concentration-time curve for the active ingredient only. This approach would enable estimates of the decomposition constant to be obtained for cases where the decomposition product is not amenable to simultaneous assay or where more than one product is formed during decomposition.

This approach may be extended to treat the dissolution process by first order kinetics and work is in progress to compare predicted and experimental rate constants determined in this manner. Such a procedure can be envisaged as finding application in preformulation studies or for pro-drugs where the rate of decomposition to an active ingredient is highly relevant when compared with the intrinsic dissolution rate.

Wood, J.H. et al (1965) J. Pharm. Sci. 54, 1068

0022-3573/82/120087P-01$02.50/0