MODELLING THE DISSOLUTION KINETICS OF IBUPROFEN

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1. Introduction

Ibuprofen is a widely used NSAID sparingly soluble at low pH. Previous studies [1, 2] showed that different dissolution rate constants are obtained, for different size fractions, when the data are plotted according to the integrated forms of the modified Noyes-Whitney equation [3]. Also linear plots were not always found. These results were, somehow, unexpected since in the derived equations the variation of particle size, as a function of time, was taken into account.
These equations are valid for monodisperse spheres. However, for multisized powders they are questionable. Therefore the model was applied to each size class of the size distribution. The purpose of this study was to compare simulated profiles, evaluated in this way, with those obtained experimentally.

2. Experimental Work

The experimental procedure adopted in this work was to follow the suspended solids concentration, as a function of time, using a Coulter Multisizer II. The size distribution of the Ibuprofen measured by this technique and used later to evaluate the dissolution profile is presented in Fig. 1.

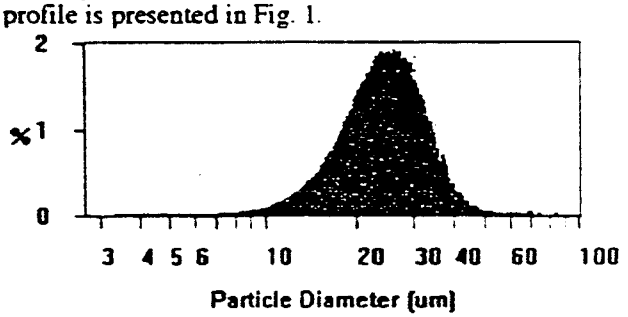

Fig.1. Particle size distribution of the Ibuprofen obtained with the Coulter Multisizer II

The particle shape factor was calculated from the powder specific surface area (BET), as described elsewhere [4]. The diffusion coefficient was calculated by the Levich equation [5] using the rotating disk method.

3. Simulation Work

Assuming the boundary layer thickness equal to the particle radius [6] and working under sink conditions, the integrated equation takes the form:

$$W_0^{2/3} - W^{2/3} = Kt \qquad (1)$$

where W_0 and W are the suspended solids weight at time t=0 and t=t, respectively, and K is the dissolution rate constant. This equation was applied to each size class (in a total of 64 classes) of the initial particle size distribution, the total mass of suspended solids, at a given time, being equal to the summation of the calculated values. The number of particles in each size class was constantly updated taking into consideration the correspondent mass decrease computed at every time interval.
Fig. 2 shows the comparison of the experimental and simulated dissolution profiles.

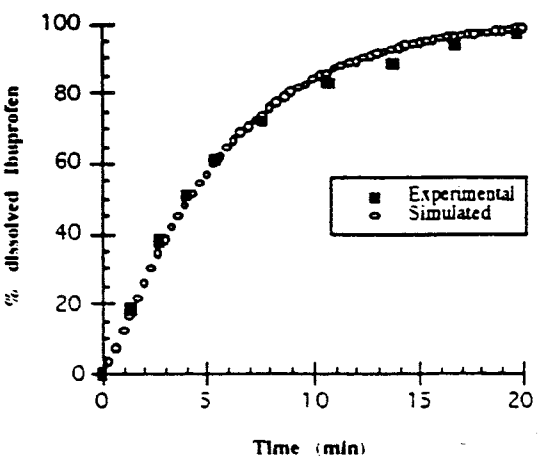

Fig.2 Comparison between experimental and simulated dissolution profiles

4. Conclusions

The simulated data are in almost perfect agreement with the experimental profile, leading to the conclusion that the methodology adopted here is valid to describe the dissolution process of Ibuprofen. Moreover, this approach has the greatest advantage of being straightforward, basically requiring the knowledge of the initial particle size distribution of the pharmaceutical powder.

References

[1] S. Simões., A. Sousa and M. Figueiredo. *Symposium on Solid Oral Dosage Forms.*; Stockholm (1994).

[2] L. Pereira de Almeida, S. Simões, A. Sousa and M. Figueiredo. *1st World Meeting on Pharmaceutics, Biopharmaceutics, and Pharmaceutical Technology*; Budapest (1995).

[3] A.A. Noyes, W.R. Whitney. *J. Am. Chem. Soc.* 19, (1987).

[4] C. Nyström, J. Mazurt, M.I. Barnett and M. Glazer. *J. Pharm. Pharmacol.* 37, 217-221 (1985).

[5] V.G. Levich. Physico-chemical Hydrodynamics. Prentice Hall, Englewood Cliffs (N.J.) (1962).

[6] R.J. Hintz, K.C. Johnson. *Int. J.Pharm.* 51, 9-17, (1989).