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# Water uptake and force development in an optimized prolonged release formulation *

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## Summary

A new prolonged release oral tablet has recently been developed. The formula, which contains an antiinflammatory agent (diclofenac sodium), two inert polymers (polyvinylchloride and ethylcellulose) and two lubricants (magnesium stearate and talc), was optimized as far as the manufacturing process was concerned. The outcome was the selection of a few optimized tablets, which were obtained by different processes (direct compression, double compression, compaction of the five raw materials, separate compaction of the drug and polyvinylchloride and wet granulation). From a biopharmaceutical point of view the response variables of major interest were dissolution profile and the variability of dissolution. In the present work, with the aim of elucidating the mechanisms of drug release, water penetration and force development measures were undertaken on the optimized tablets and related to porosimetry data. Differences between the various tablets were found both in water uptake and force development. The rate of water penetration may be related to tablet porosity and pore size for the formulations obtained by direct compression, double compression and compaction. However, the influence of simultaneously occurring phenomena, such as dissolution and/or pore widening, must be taken into account. In the case of wet granulation the water penetration rate is lower than expected on the basis of tablet porosity, due to the presence of the binder. The variability of the water penetration rate is related to the variability of mean pore diameter. As expected, the kinetics of force development is related to the kinetics of water uptake. Water penetration and force development studies proved useful to elucidate the microstructure of the tablets and to understand the interactions between water and polymeric chains: these interactions may in part explain the release pattern that is observed during dissolution tests.

## Introduction

A new prolonged release tablet has recently been developed (Pena Romero et al., 1988a,b, 1989a,b,c). The formula, which contains an antiinflammatory agent (diclofenac sodium), two in-

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ert polymers (polyvinylchloride and ethylcellulose) and two lubricants (magnesium stearate and talc), was chosen on the basis of preliminary studies on aptitude for compression and prolongation of release (Pena Romero et al., 1988a).

The formula was then optimized as far as tablet weight and percent composition (Pena Romero et al., 1988b) and manufacturing process (Pena Romero et al., 1989a,b,c), were concerned. Among the optimized responses dissolution profile and the variability of dissolution were considered.

The outcome was the selection of a few optimized tablets that were obtained by different processes: direct compression, double compression, compaction of the mixture of the five components, separate compaction of the active principle (AP) and polyvinylchloride (PVC) and wet granulation.

Subsequently the search for the best process was effected on the basis of the rheological properties of the mixture of the components (either granulated or not), tablet microstructure and the variability of dissolution (Pena Romero et al., 1990). To explain differences in dissolution profiles and dissolution variability and to substantiate the choice of the best process, porosity measurements were also performed on each optimized formulation. The best process was found to be wet granulation. Moreover, a rank order correlation was found between the variability of mean pore diameter and the variability of dissolution efficiency for all the tested tablets (Pena Romero et al., 1990).

Although porosity is definitely a relevant factor in the drug release process, other properties, such as contact angle, pore structure and pore structure changes upon water contact, may influence water penetration and the subsequent drug diffusion out of the matrices.

In the present paper, in order to exploit porosimetry data, water uptake measurements have been undertaken on the optimized tablets.

Water uptake measurements have been extensively employed to explain the phenomenon of disintegration in fast disintegrating tablets (Couvreur et al., 1975; Ringard et al., 1977; Bolhuis et al., 1982; Caramella et al., 1986) and to elucidate the relationships between disintegration and dissolution in soluble tablet formulations (Van Kamp et al., 1986a).

Water uptake has also been studied on inert polymer matrices, where it is generally accepted that liquid penetration is the first, although not necessarily the limiting step, in the drug release process. In particular, water uptake into inert polymer matrices was related to pore structure and wettability, also depending on polymer nature and its interaction with the penetrating liquid (Carli and Simioni, 1978). Indeed, water uptake was not necessarily related to the mechanism of drug release, which mainly depended on the subsequent drug diffusion (Carli et al., 1983).

In the case of the tablets that are examined in the present paper, there was also some evidence of erosion and disintegration during the release test, which could be relevant to the release process (Pena Romero et al., 1990). Therefore it was conceivable that water uptake studies should provide information about the evolution of porosity and pore size during water penetration and their possible relevance towards the release process. Moreover, given the fact that the active principle (diclofenac sodium) is characterized by a pH-dependent solubility, it was thought useful to perform liquid penetration measurements in different pH conditions.

Another phenomenon that is usually believed to provide valuable information on the interactions between polymeric excipients and penetrating liquid is the development of force inside compacts. This force may be due to polymer swelling or to any other kind of interaction between polymeric chains and penetrating liquid, which in turn may be responsible for tablet disruption and/or erosion.

Although extensively performed in the case of fast disintegrating tablets (Caramella et al., 1988, 1989), the study of force development in inert matrices is rather new. In view of that, force development measures have also been undertaken on each optimized tablet.

The overall evaluation of water uptake and force development data should provide information on how water-polymer interactions do change depending on tablet structure (porosity, pore size), how force development is related to water penetration and how the two measurements contribute to the explanation of the release process.

## Experimental

### *Tested formulations*

The composition of the examined tablets is given in Table 1 (Pena Romero et al., 1989c). The different manufacturing processes used are briefly recalled:

(1) Direct compression: direct compression of the whole formula using either a rotative or an alternative tableting machine (Pena Romero et al., 1988b).

(2) Double compression: precompression of diclofenac sodium, polyvinylchloride and one half of ethylcellulose, regranulation before mixing with the second part of ethylcellulose and lubricants, final compression with an alternative press (Pena Romero et al., 1989a).

(3) Compaction of the mixture: compaction of the ingredients, except one half of the lubricants, in a rotating cylinder press; regranulation and mixing with the second part of the lubricants; final compression with an alternative press (Pena Romero et al., 1990).

(4) Separate compaction of diclofenac sodium and polyvinylchloride: separate compaction of the active principle and polyvinylchloride; regranulation and mixing with the remaining ingredients and final compression with an alternative press (Pena Romero et al., 1989b).

(5) Wet granulation: granulation of the ingredients (diclofenac sodium and the two polymers) with an appropriate binder solution; lubrication and final compression with an alternative press (Pena Romero et al., 1989c).

The compression force used and the porosimetry parameters of the examined tablets are reported in Table 2 (Pena Romero et al., 1990).

TABLE 1

*Optimized tablet composition (% w / w)*

| | |
|---|---|
| Diclofenac sodium [a] | 25.0% |
| Ethylcellulose [b] | 26.1% |
| Polyvinylchloride [c] | 45.9% |
| Talc [d] | 2.0% |
| Magnesium stearate [e] | 1.0% |

[a] Mean diameter, 105 μm; water solubility, 100 mg/ml (Secifarma).

[b] Mean diameter, 145 μm; ethylcellulose EC N-7 (Hercules).

[c] Mean diameter, 250 μm; Pevikon PE 737® (Seppic).

[d] (Prophac).

[e] (Prophac).

### *Methods*

*Water uptake measurements.* Liquid uptake measurements were performed using the apparatus previously described (Van Kamp et al., 1986b) and subsequently modified (Ferrari et al., 1988). Measurements were carried out with distilled water, with hydrochloric acid (0.1 N) and with phosphate buffer ($pH = 6.8$) in controlled temperature and relative humidity conditions. To quantify weight loss due to water evaporation during liquid uptake, blank measurements were effected in the same experimental conditions as with the tablets. The weight loss (mean of three replicates) due to evaporation showed a linear kinetics and was subtracted from the experimental data by the computer.

Liquid uptake data were collected and stored in the memory of a personal computer (IBM AT, 512 kbytes) to allow subsequent fitting according to appropriate models. The modelling was performed with a non-linear regression procedure using a commercial package (SIPHAR®, Simed, Créteil, France).

In the majority of cases fitting of water uptake data was performed using the '$E_{max}$ model' (SIPHAR® User's Manual). This model comes in different versions, which allows maximum flexibility in fitting of water penetration curves (Ferrari et al., 1991). The version employed was the 'sum of two $E_{max}$' model. This model allows the possible presence of two simultaneously occurring processes, both contributing to the overall water penetration phenomenon, to be evidenced. Each process is characterized by a set of parameters: a slope (sigmoidicity) parameter ($\gamma$) that describes the shape of the curve and a time parameter ($t_{50}$) that represents the time needed for uptaking

50% of the total water amount through the process considered. The model is described by the following equation:

$$Q = Q_{\max}\left(\frac{t^{\gamma_1}}{t_{50_1}^{\gamma_1} + t^{\gamma_1}} + \frac{t^{\gamma_2}}{t_{50_2}^{\gamma_2} + t^{\gamma_2}}\right) \qquad (1)$$

where $Q$ is the amount of liquid uptake at time $t$ (mg), $Q_{\max}$ is the total (maximum) amount of liquid uptake by the end of the experiment (mg), $\gamma_1$ and $\gamma_2$ are slope (sigmoidicity) factors of the two processes, and $t_{50_1}$ and $t_{50_2}$ represent the time needed for uptake of 50% of the total liquid amount through the two processes (min).

The goodness of fit was established on the basis of the statistical parameters of the model: the coefficient of determination ($R^2$), the sum of squares of the differences between fitted and experimental data (SSQ) and the percent coefficient of variation of the estimated parameters.

In a few cases liquid uptake data were fitted using a classical exponential model (Weibull), as already proposed (Ferrari et al., 1988), according to the following equation:

$$Q = Q_{\max}\left(1 - \exp^{-(t - t_0/t_{50})^{\beta}}\right) \qquad (2)$$

where $Q$ is the amount of liquid uptake at time $t$ (mg), $Q_{\max}$ is the total (maximum) amount of liquid uptake by the end of the experiment (mg), $t_0$ is lag time (min), $t_{50}$ is the time needed for uptake of 50% of the total liquid amount (min), and $\beta$ is a shape parameter.

From the model parameters secondary parameters were derived. In particular the first derivative of the curve at $t_{50}$ was calculated. This parameter, named Input$_{(50)}$, represents an instantaneous rate of water uptake and may be used for describing the overall kinetics of the water uptake process.

In the case of the curves fitted with the 'sum of two E$_{\max}$' model, which allows the differentiation of two distinct processes (see Eqn 1), two distinct instantaneous rate parameters (Input$_{(50)_1}$ and Input$_{(50)_2}$), that are the derivatives of the two modeled processes at $t_{50_1}$ and $t_{50_2}$, respectively, were calculated. The instantaneous rate parameters, together with $\gamma_1$ and $\gamma_2$, should enable a comparative evaluation of the contribution of the two processes to the overall phenomenon of water uptake (Ferrari et al., 1991). The uncertainty of the secondary parameter(s) was estimated using the theory of propagation of errors (Berington, 1969). Moreover, the percent thickness in-

TABLE 2

*Synoptic table of tablet properties (C.V., coefficient of variation of three replicates)*

| Process | Compression force (kN) | Porosity % (C.V. %) | Pore volume ($cm^3$/tablet) (C.V. %) | Mean pore diameter ($\mu$m) (C.V. %) |
|---|---|---|---|---|
| Direct compression | | | | |
| Alternative | 7 | 33.8 | 0.134 | 0.230 |
| | | (2.1) | (3.3) | (11.5) |
| Rotative | – | 28.8 | 0.108 | 0.152 |
| | | (6.1) | (9.3) | (26.8) |
| Double compression | 12 | 23.7 | 0.083 | 0.068 |
| | | (2.8) | (2.8) | (4.2) |
| Compaction of the mixture | 31 | 16.6 | 0.053 | 0.022 |
| | | (3.9) | (3.7) | (4.5) |
| Separate compaction of AP and PVC | 19 | 21.8 | 0.074 | 0.057 |
| | | (6.0) | (7.1) | (17.4) |
| Wet granulation | 7 | 32.8 | 0.124 | 0.252 |
| | | (1.9) | (2.6) | (6.4) |

crease of each tablet was evaluated at the end of the water uptake experiment.

*Force development measures.* Force development measures were performed as previously described (Colombo et al., 1980). Measures were effected on all the tablets with the exception of those prepared on the rotative tableting machine on which force measurements were not feasible owing to their shape.

Force development versus time data were fitted according to the Weibull model in the following form:

$$F = F_{\max}\left(1 - \exp^{-(t-t_0/t_{50})^{\beta}}\right) \qquad (3)$$

where $F$ is the amount of force developed at time $t$ (N), $F_{\max}$ is the maximum amount of force developed by the end of the experiment (N), $t_0$ is lag time (min), $t_{50}$ is the time needed to reach 50% of maximum force developed (min), and $\beta$ is a shape parameter.

In analogy with water uptake, the first derivative of force development curves at $t_{50}$ was evaluated, which was named $\text{Input}_{(50)\ \text{force}}$.

## Results and Discussion

Water uptake profiles of the examined tablets are given in Fig. 1. It may be appreciated that the different tablets markedly differ not only for the total amount of water uptake, but also for the kinetics of water penetration.

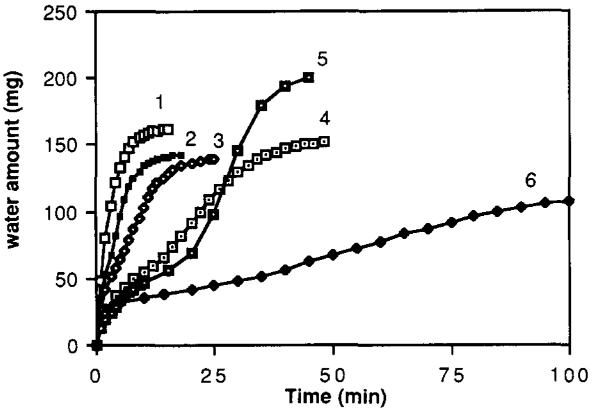

Fig. 1. Water uptake profiles of six tablets. 1, direct compression (alternative); 2, direct compression (rotative); 3, double compression; 4, compaction of the mixture; 5, separate compaction of AP and PVC; 6, wet granulation.

Liquid uptake profiles in hydrochloric acid (0.1 N) or phosphate buffer (pH 6.8) were slightly different from those obtained in distilled water, but the rank order in penetration rate among the various tablets was maintained.

As an example, liquid uptake profiles obtained in hydrochloric acid for some of the tablets examined are shown in Fig. 2. The similarity of these curves to those given in Fig. 1 indicates that the solubility of the active principle in the penetrating liquid hardly influences the liquid penetration.

The most significant water uptake data are summarized in Table 3. For all the tablets examined, with the exception of those obtained by wet granulation, the maximum amount of water uptake (mg/tablet) exceeds the total pore volume ($\text{cm}^3$/tablet) as obtained from porosimetry (Table 2). This is due to pore widening during water penetration, which in turn may be due to the partial disintegration of the matrix.

The disintegration propensity is also indicated by the eventual percent increase in tablet thickness (Table 3). This increase is particularly evident for the tablets obtained by compaction of the components, which could possibly be linked to the high compression force (Table 2) as well as to the different distribution of the polymers inside this matrix.

As for process kinetics, with the exception of tablets obtained by direct compression (alternative tableting machine), whose water uptake curves are well described by a simple exponential equation (Weibull), for all the other tablets, which showed a biphasic pattern in the water uptake curves (Fig. 1), a more complicated model (that is the 'sum of two $E_{\max}$' model) was needed for an adequate fit of experimental data. Best fit parameters of the water uptake curves that were fitted according to the 'sum of two $E_{\max}$' model are given in Table 4.

Two processes are distinguishable from a mathematical modelling point of view. In fact, two different sigmoidicity factors ($\gamma_1$ and $\gamma_2$) and two different rate parameters ($\text{Input}_{(50)_1}$ and In-

TABLE 3

*Water uptake data (C.V., coefficient of variation of three replicates)*

| Process | Maximum water uptake (mg) (C.V. %) | % thickness increase (C.V. %) | Input$_{(50)}$ [a] (mg/min) (C.V. %) |
|---|---|---|---|
| Direct compression | | | |
| Alternative | 161 | 13.4 | 29.88 (a) |
| | (4.6) | (2.68) | (7.18) |
| Rotative | 139 | 13.4 | 13.63 (b) |
| | (2.7) | (2.71) | (9.07) |
| Double compression | 138 | 15.2 | 7.28 (b) |
| | (4.8) | (1.44) | (5.62) |
| Compaction of the mixture | 153 | 22.1 | 4.09 (b) |
| | (9.9) | (2.12) | (1.96) |
| Separate compaction of AP and PVC | 197 | 24.5 | 9.02 (b) |
| | (10.7) | (9.43) | (25.83) |
| Wet granulation | 109 | 5.1 | 0.97 (b) |
| | (4.9) | (8.43) | (3.16) |

[a] Instantaneous rate parameter calculated from curves fitted according to Weibull model (a) and according to 'sum of two $E_{max}$' model (b).

The coefficient of determination ($R^2$) was higher than 0.99. Uncertainty of parameter estimate (expressed as percent coefficient of variation of estimated parameter) was less than 15% (except in the case of separate compaction of AP and PVC for which it ranged between 20 and 30%).

put$_{(50)_2}$) were estimated by the best fit procedure. Therefore it may be envisaged that two different processes, possibly corresponding to two different mechanisms of water uptake, simultaneously contribute to the overall phenomenon of water penetration. There could be, for example, a slow capillary penetration accompanied by a process of pore widening which triggers a more rapid water penetration.

The occurrence of two different processes, characterized by two significantly different rate parameters, is particularly evident in the case of the tablets obtained by separate compaction (Table 4). It is conceivable that the process associ-

TABLE 4

*Best fit [a] parameters of water uptake profiles (fitting according to 'sum of two $E_{max}$' model) (C.V., coefficient of variation of three replicates)*

| Process | $\gamma_1$ (C.V. %) | $\gamma_2$ (C.V. %) | Input$_{(50)_1}$ (mg/min) (C.V. %) | Input$_{(50)_2}$ (mg/min) (C.V. %) |
|---|---|---|---|---|
| Direct compression (rotative) | 3.63 | 1.35 | 10.86 | 17.42 |
| | (10.74) | (3.42) | (12.69) | (27.53) |
| Double compression | 3.93 | 1.21 | 7.07 | 12.47 |
| | (3.42) | (17.38) | (13.65) | (38.46) |
| Compaction of the mixture | 4.36 | 0.89 | 3.85 | 3.54 |
| | (2.48) | (21.45) | (7.37) | (22.89) |
| Separate compaction of AP and PVC | 7.84 | 0.70 | 9.03 | 0.97 |
| | (32.73) | (5.02) | (29.78) | (17.63) |
| Wet granulation | 0.24 | 2.86 | 0.20 | 0.86 |
| | (25.34) | (11.42) | (121.82) | (70.70) |

[a] The coefficient of determination ($R^2$) was higher than 0.99. Uncertainty of model parameter estimate (expressed as percent coefficient of variation of estimated parameters) was less than 15%.

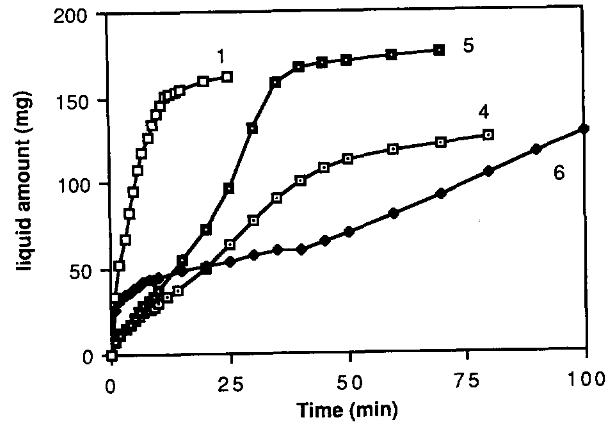

Fig. 2. Liquid uptake profiles of four tablets in 0.1 N HCl. 1, direct compression (alternative); 4, compaction of the mixture; 5, separate compaction of AP and PVC; 6, wet granulation.

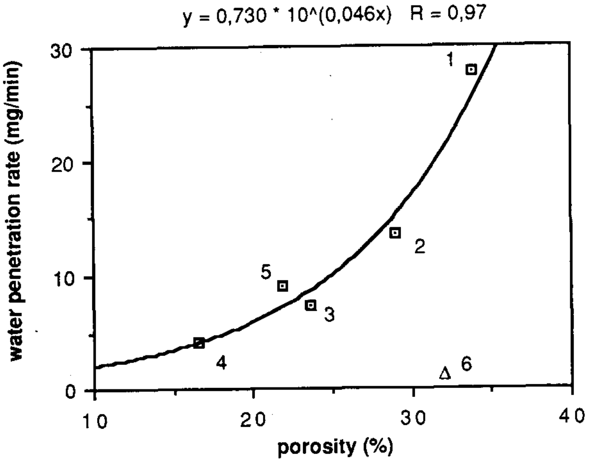

Fig. 3. Relationship between water penetration rate ($\mathrm{Input}_{(50)}$, mg/min) and tablet porosity (%). 1, direct compression (alternative); 2, direct compression (rotative); 3, double compression; 4, compaction of the mixture; 5, separate compaction of AP and PVC; 6, wet granulation. $\Delta$, not entered in the regression equation.

ated with the highest rate parameter ($\mathrm{Input}_{(50)_1}$ = 9.03 mg/min) is the major responsible one for water penetration; this process probably corresponds to the sudden pore widening that takes place after an initial slower capillary penetration. This result both confirms and explains the biphasic pattern that has been observed in liquid penetration curves (see patterns 5 in Figs 1 and 2).

In the case of the other tablets the differences between the two rate parameters ($\mathrm{Input}_{(50)_1}$ and $\mathrm{Input}_{(50)_2}$) are less marked, meaning that also the differences between the two underlying processes are less marked.

As for the relationships between water penetration and tablet porosity, no correlation whatsoever has been found between porosity percentage (Table 2) and total amount of water uptake (Table 3). For example, in the case of the tablets obtained by wet granulation, which are characterized as the ones with the highest porosity value, the lowest amount of water uptake has been observed. Nevertheless, an exponential relationship has been found (Fig. 3) between instantaneous water penetration rate ($\mathrm{Input}_{(50)}$) and porosity percentage. At an even higher significance level, a linear relationship has been found (Fig. 4) between water penetration rate and mean pore diameter. The existence of these relationships confirms that porosity and pore size distribution determine the rate of water penetration rather than the total amount of water uptake.

These two relationships concern the tablets that are obtained by direct compression, double compression or compaction; in the case of wet granulation, water penetration is slower than ex-

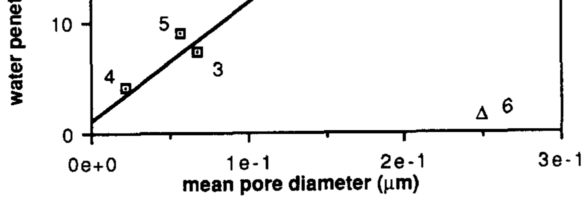

Fig. 4. Relationship between water penetration rate ($\mathrm{Input}_{(50)}$, mg/min) and mean pore diameter ($\mu$m). 1, direct compression (alternative); 2, direct compression (rotative); 3, double compression; 4, compaction of the mixture; 5, separate compaction of AP and PVC; 6, wet granulation. $\Delta$, not entered in the regression equation.

pected on the basis of porosity percentage and mean pore diameter, due to the presence of the binder, which not only changes wettability properties but also is likely to hinder tablet expansion.

A linear relationship has also been found (Fig. 5) between the variability of water penetration, as expressed by the coefficient of variation of the instantaneous rate of the water uptake parameter ($\text{Input}_{(50)}$) and the variability of mean pore diameter, as expressed by its coefficient of variation. This is in line with the rank order correlation that had been found between the variability of mean pore diameter and the variability of dissolution efficiency for all the tested tablets (Pena Romero et al., 1990). This indicates that water penetration may, at least in part, explain the variability of dissolution.

Force development inside the inert matrices examined may be explained by the presence of ethylcellulose and attributed to the interaction between water and the hydrophilic portions of polymer chains. In fact force measurements effected on pure ethylcellulose tablets showed that this polymer is capable of developing a force upon contact with water (Fig. 6).

The force parameters of the five matrices examined are given in Table 5. It must be pointed out that, unlike in the case of fast disintegrating tablets (Colombo et al., 1984), the relationships between compression force (Table 2) and the amount of force developed or the rate of force development (Table 5) are not that evident, meaning that the force development is linked not only to the bond strength but also to the polymer distribution inside the matrices.

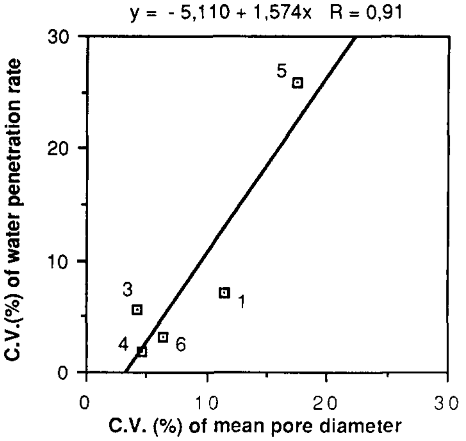

Fig. 5. Relationship between variability in water penetration rate (C.V.% of $\text{Input}_{(50)}$) and variability in mean pore diameter (C.V.%). 1, direct compression (alternative); 3, double compression; 4, compaction of the mixture; 5, separate compaction of AP and PVC; 6, wet granulation.

A linear correlation exists between force development rate and water penetration rate (Fig. 7). Such a correlation might be expected as long as water entrance into tablets during force experiments were not impaired by some reasons. It must be pointed out that data relative to the tablets that were prepared by separate com-

TABLE 5

*Best fit* [a] *parameters of force development curves (fitting according to Weibull model) (C.V., coefficient of variation of three replicates)*

| Process | $F_{\max}$(N) (C.V. %) | $t_{50}$ (C.V. %) | $\beta$ (C.V. %) | $\text{Input}_{(50)\,\text{force}}$ (N/min) (C.V. %) |
|---|---|---|---|---|
| Direct compression (alternative) | 28.35 | 1.04 | 1.10 | 10.29 |
| | (10.01) | (8.38) | (4.72) | (2.52) |
| Double compression | 27.57 | 3.20 | 1.25 | 3.72 |
| | (4.42) | (9.85) | (8.05) | (2.64) |
| Compaction of the mixture | 38.32 | 10.12 | 1.15 | 1.50 |
| | (8.45) | (9.73) | (11.21) | (11.92) |
| Separate compaction of AP and PVC | 15.91 | 17.37 | 1.19 | 0.44 |
| | (26.89) | (18.41) | (9.36) | (15.13) |
| Wet granulation | 8.20 | 18.06 | 0.76 | 0.13 |
| | (6.98) | (32.03) | (6.22) | (33.53) |

[a] The coefficient of determination ($R^2$) was higher than 0.99. Uncertainty of model parameter estimate (expressed as percent coefficient of variation of estimated parameters) was always less than 10%.

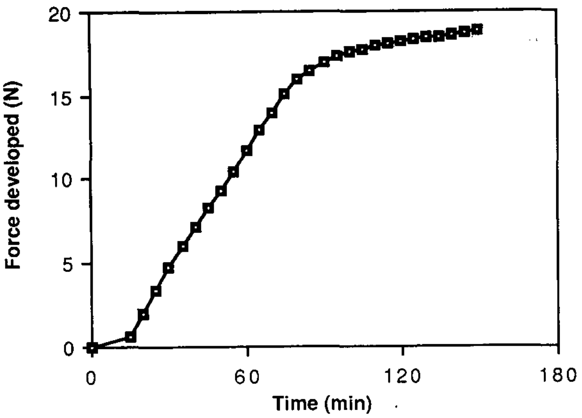

Fig. 6. Disintegrating force developed by an individual ethylcellulose tablet.

paction are outside this correlation. In fact, in this case, water entrance during force measurements is impaired possibly due to pore blockade, which restricts the amount of water eventually taken up by the tablet (this phenomenon was also confirmed by performing experiments with a coloured water solution). The low amount of water taken up during the force experiment is responsible for the unexpectedly low force measured. The pore blockade may be caused by the marked disintegration propensity shown by this tablet, which in turn may be linked to the peculiar distribution of the hydrophilic polymer (ethylcellulose) inside this matrix.

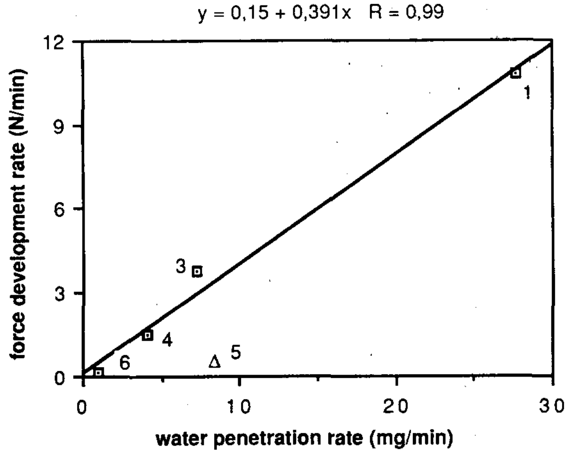

Fig. 7. Relationship between water penetration rate (Input$_{(50)}$, mg/min) and force development rate (Input$_{(50)\ \mathrm{force}}$, N/min). 1, direct compression (alternative); 3, double compression; 4, compaction of the mixture; 5, separate compaction of AP and PVC; 6, wet granulation. $\Delta$, not entered in the regression equation.

Finally, as for the possible relationship between water penetration rate and dissolution pattern (Pena Romero et al., 1990), things tend to be more complicated. It must be taken into account that, although water penetration is the first step in drug release, drug dissolution is mainly limited by drug diffusion out of the matrix.

However, the different behavior of the tablet upon water entrance, especially pore widening and subsequent tablet opening, explains in part the sigmoidal pattern of dissolution curves of certain formulations (for example double compression and compaction) (Pena Romero et al., 1990).

For wet granulation tablets the pronounced sigmoidicity in dissolution profiles is in line with the disintegration tendency that is observed in the dissolution medium (Pena Romero et al., 1990) although no such behavior could be appreciated in water penetration experiments, possibly due to the different experimental conditions with respect to the dissolution test.

## Conclusions

Water penetration and force development studies proved useful to elucidate the microstructure of the tablets and to understand the interactions between water and polymeric chains: these interactions may in part explain the release pattern that is observed during dissolution tests.

It is the first time that both water uptake and force measurements have been effected on inert matrices. It is conceivable to point out that force measurements on matrices that are based on hydrophilic although water insoluble polymers (like ethylcellulose) can be exploited to elucidate water-polymer interactions.

By the way, it is felt that some of the results achieved in the case of fast disintegrating tablets (Caramella et al., 1986) are also confirmed in the case of slowly eroding and slowly disintegrating compacts: in particular, as expected, the kinetics of force development are related to the kinetics of water uptake.

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