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# Selective coating of cylindrical matrices with a central hole. II. An interpretation of the release process

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## Summary

A swellable perforated matrix was prepared and coated on one or more of its surfaces. Two drugs having different water solubility were chosen to load the matrix. To clarify the effect of the matrix swelling on the release process, the release rate was analysed according to the swelling area, i.e., the surface area from which the drugs could be released. According to the experimental release data, the drug solubility usually predominated at the beginning and the matrix swelling at the end of the release process. When the interior hole was the only uncoated surface, pseudo-zero order kinetics were obtained when the drug solubility allows the control of the drug release by the matrix swelling.

## Introduction

A variety of approaches were proposed for the preparation of controlled release matrices. Among these, two rewarding approaches aroused our interest.

The first concerns the coating of appropriate surfaces of a cylindrical swellable matrix (Colombo et al., 1990), the second involving the modification of the matrix geometry by boring a hole in the centre of the flat surface through both sides of the cylindrical matrix (Cleave, 1965). While the major effort was focused on the development of non-swellable perforated tablets or matrices (Hsieh et al., 1983; Hansson et al., 1988; Forni et al., 1990), much less emphasis has been extended to combine the advantages of the selective coating with those of the swellable perforated matrices. To achieve this purpose, a swellable perforated matrix was prepared and coated on one or more of its surfaces. Two drugs having different water solubility were chosen to load the matrices.

In a previous work (Vandelli and Cameroni, 1993), the swelling process of the perforated matrices was studied according to the selective coating (the number and the position of the coated surfaces) and the drug solubility. The selective coating modified the water penetration and acted as a mechanical hindrance forcing the particles to swell in preferential directions. Thus, the swelling

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kinetics of the uncoated matrices changed according to the selective coating and the drug solubility. When the surface of the internal hole was the only one uncoated, the matrices swelled following pseudo-zero order kinetics regardless of the loaded drug.

This contribution attempts to investigate the influence of selective coating on the release of two drugs with different water solubility (sodium salicylate or theophylline). This paper is also aimed at clarification of the influence of the above factors (selective coating and drug solubility) on the role of the matrix swelling in the release from such delivery systems.

## Experimental

### *Materials*

Sodium salicylate (NaS) (USP, Carlo Erba, Milan, Italy; Mol. Wt 160.1; water solubility 1 g $ml^{-1}$) and theophylline (Theo) (USP, Carlo Erba; Mol. Wt 198.2; water solubility $8.3 \times 10^{-3}$ g $ml^{-1}$) were used. Polyvinyl alcohol (PVA) (polyvinyl alcohol 100000, Fluka, Buchs, Switzerland) (viscosity of a 4% water solution at 20°C, 35–45 mPa s; degree of polymerisation, 2000; degree of hydrolysis, 86–89 mol%) was the excipient. The drugs and the excipient were separately ground (Pulverisette 0, Fritsch, Idar-Oberstein, Germany) and sieved (Harver and Boecker, Oelde, Germany) before matrix preparation. The granulometric fraction between 90 and 125 $\mu$m was used. Cellulose acetate phthalate (Fluka) and diethyl phthalate (Fluka) were used to coat the matrices as received from the manufacturer. All the solvents were of pure grade (Carlo Erba).

### *Methods*

#### *Preparation of the uncoated matrices*

The cylindrical matrices (matrices A1) (weight, $420 \pm 5$ mg; diameter ($d_e$), $13 \pm 0.2$ mm; thickness ($h$), $2.9 \pm 0.1$ mm) were prepared by compression of a homogeneous mixture of the drug (NaS or Theo) and the excipient (PVA) (drug/PVA ratio, 1:9 w/w) as previously described (Vandelli and Cameroni, 1993). The perforated matrices (matrices A2) (weight, $420 \pm 5$ mg; $d_e$, $13 \pm 0.1$ mm; $h$, $3.8 \pm 0.1$ mm) were obtained boring a hole (diameter ($d_e$), $5 \pm 0.1$ mm) in the centre of the flat surface through both sides of a cylindrical matrix weighing $450 \pm 5$ mg (Vandelli and Cameroni, 1993). The matrix geometry and code are reported in Fig. 1.

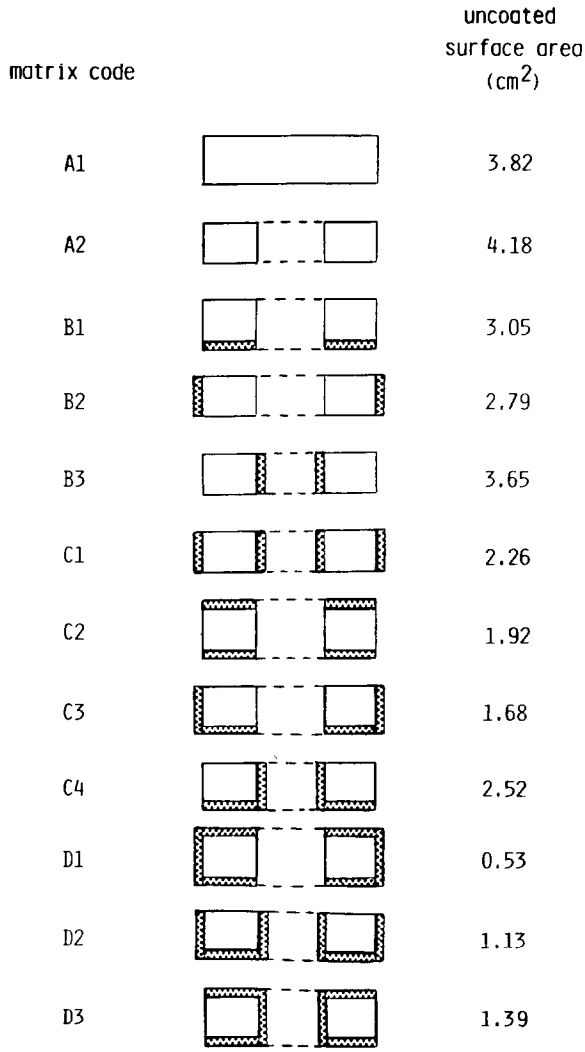


Fig. 1. Matrix geometry, code and uncoated surface area of the different matrices.

#### *Coating of the perforated matrix*

The perforated matrix was coated on one (matrices B), two (matrices C), or three (matrices

D) surfaces (Fig. 1) as previously described (Vandelli and Cameroni, 1993). The coating of all the surfaces of a perforated matrix did not allow the release of the drugs under the experimental conditions.

*Drug release from the matrices*

Drug release from the matrices was examined using a column-type apparatus (Dissotest CE-1, Sotax, Basel, Switzerland) in 1000 ml deionized water at a flow rate of 25 ml $min^{-1}$. All experiments were carried out under sink conditions at a temperature of $37 \pm 0.2$°C. Drug content in the solution was determined spectrophotometrically (model Lambda 3A, Perkin-Elmer, Norwalk, U.S.A.) at fixed time intervals and a suitable wavelength (230 nm for NaS; 272 nm for Theo).

*Drug release analysis*

The release kinetics of the matrices was evaluated according to the power-law expression (Ritger and Peppas, 1987):

$$M_t/M_\infty = kt^n \quad (1)$$

where $M_t/M_\infty$ is the drug amount released at time $t$, $k$ denotes the kinetic constant of release and $n$ is the kinetic exponent characterising the release mechanism.

According to Eqn 1 the release rate is defined as:

$$dM_t/d_t = nM_\infty kt^{n-1} \quad (2)$$

## Results and Discussion

The release profiles of NaS and Theo from the matrices are depicted in Figs 2 and 3. The release of NaS was greater than that of Theo for all the matrices (cylindrical, perforated, uncoated or coated).

The release of both drugs was greater from the perforated A2 than from the cylindrical A1 matrices, the difference for Theo release being the highest (Fig. 2). Thus, the uncoated matrices loaded with NaS (cylindrical or perforated)

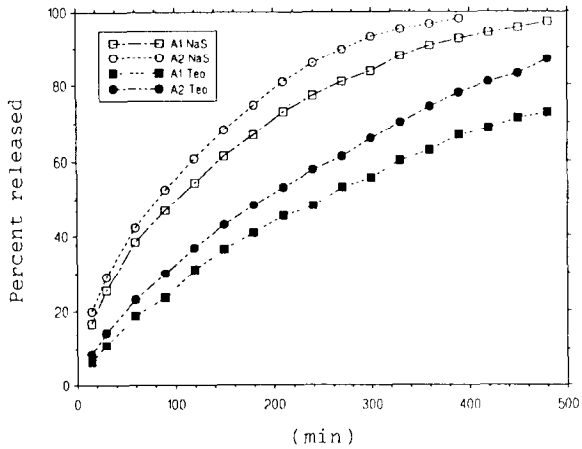


Fig. 2. Release profiles of sodium salicylate (NaS) and theophylline (Theo) from the uncoated cylindrical and perforated matrices. Codes are defined in Fig. 1.

showed practically the same instantaneous release rate (IRR), whereas Theo release was faster from the perforated than from the cylindrical matrices (Fig. 4a). The value of the kinetic exponent of drug release ($n$) was the same irrespective of the matrix geometry (cylindrical or perforated) and changed according to the loaded drug (Table 1).

Obviously, the coating of only one surface (matrices B) of the perforated matrix decreased the surface area from which water could penetrate into the dry matrix. The decrease in the uncoated surface area did not produce the same effect on the release of NaS or Theo. In fact, the release profiles of NaS from the B matrices (Fig. 3a) were closer to that of the uncoated A2 matrix than those of A2 and B2 matrices loaded with Theo (Fig. 3d).

When the perforated matrix was coated on two (matrices C) or three surfaces (matrices D), the release profiles of both drugs changed according to the position of the coated surfaces (Fig. 3b and c). The release of both drugs from C and D matrices could be related to the uncoated surface area of the dry matrix except for the NaS release from the C4 matrix. In fact, the C1 and C2 matrices showed about the same NaS release which was greater than that from the C4 matrix,

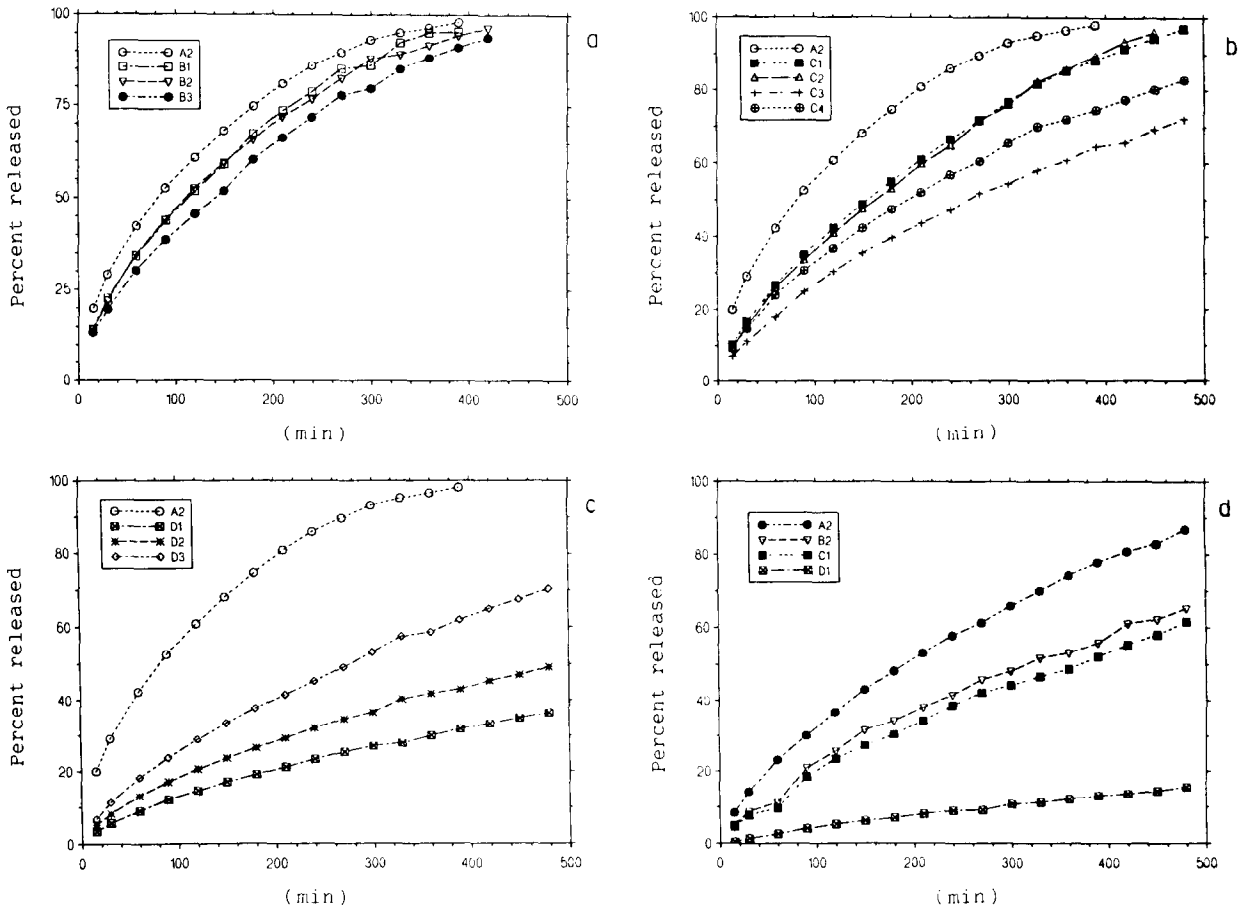


Fig. 3. Release profiles from the coated perforated matrices of sodium salicylate (NaS) ((a) matrices B; (b) matrices C; (c) matrices D] and (d) theophylline (Theo)). Codes are defined in Fig. 1.

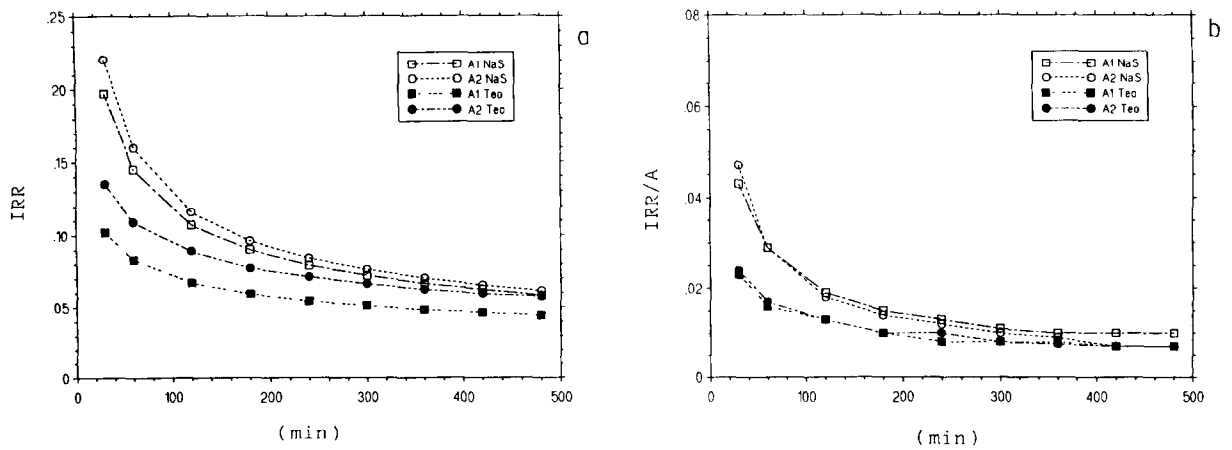


Fig. 4. Instantaneous rate of release (IRR) and instantaneous rate of release per unit swelling area (IRR/$A$) of sodium salicylate (NaS) and theophylline (Theo) from the uncoated cylindrical and perforated matrices. Codes are defined in Fig. 1.

in spite of the latter having the greatest uncoated surface area. Therefore, by coating a perforated matrix, drug release cannot be entirely related to the uncoated surface area.

The values of the kinetic exponent of both drugs were anomalous (Table 1). A shift of the $n$ value towards that typical of pseudo-zero order kinetics was demonstrated when the matrices were loaded with Theo. Thus, it could be hypothesised that the matrix geometry affects the release process. In contrast, the kinetic exponent of NaS remained unaffected by the matrix geometry. Therefore, the selective coating of the perforated matrix modified the kinetics of the release process according to the drug.

The instantaneous release rate (IRR) profiles of the drugs (NaS or Theo) from the coated matrices were different, likely owing to both the drug and the selective coating (Fig. 5a and c). Usually, the IRR values decreased as the time increased, the decrease being less evident for the matrices coated on two or three surfaces loaded with Theo (Fig. 5c). As far as the D1 matrix is concerned, the IRR values remained constant when the matrix was loaded with Theo and decreased when NaS was the loaded drug. As the D1 matrices swelled following pseudo-zero order kinetics regardless of the drug (Vandelli and Cameroni, 1993), the constant release of Theo cannot be the mere effect of the selective coating.

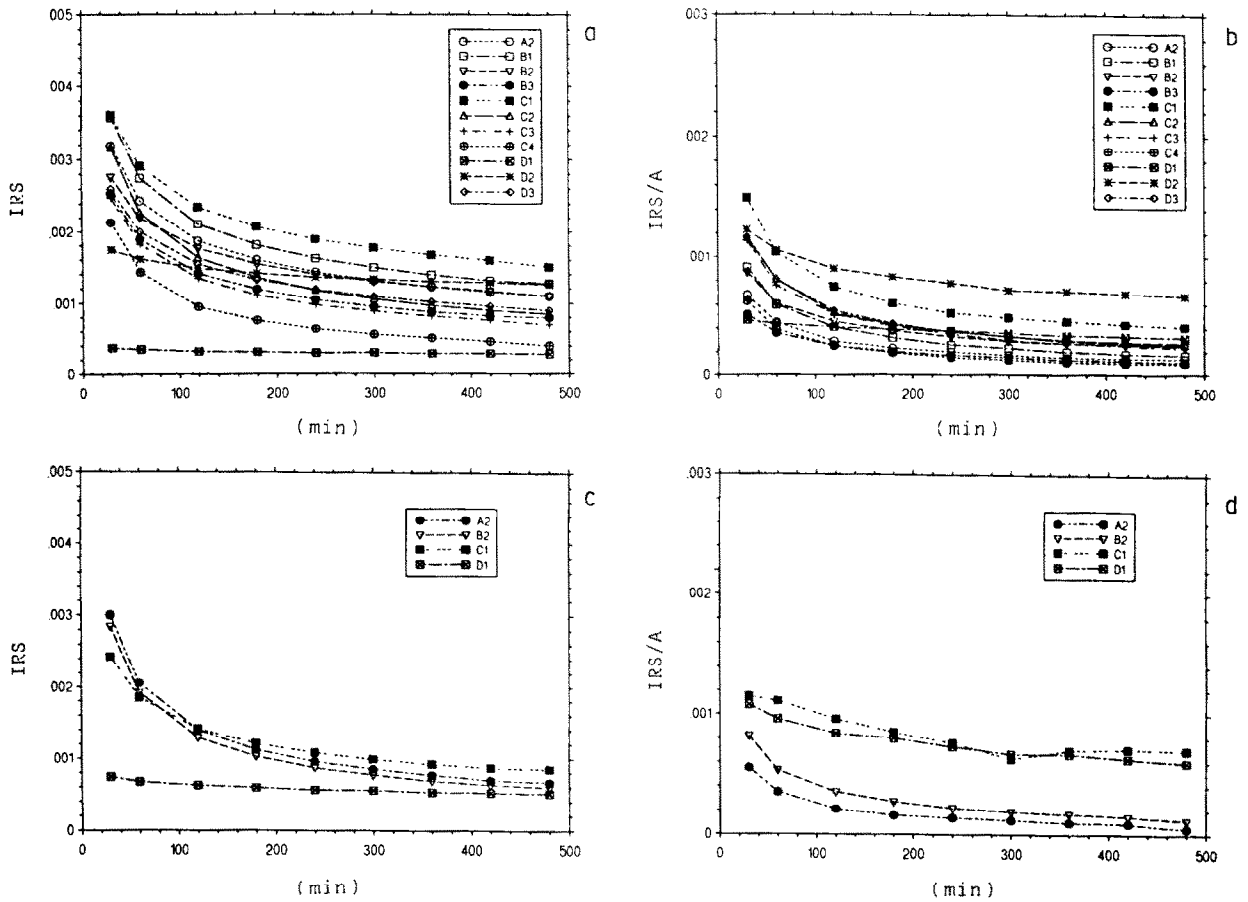


Fig. 5. Instantaneous rate of release (IRR) and instantaneous rate of release per unit swelling area (IRR/$A$) of sodium salicylate (NaS) (a,b) and theophylline (Theo) (c,d) from the coated perforated matrices. Codes are defined in Fig. 1.

TABLE 1

*Parameters of the release process from the PVA cylindrical and perforated matrices calculated according to the power-law expression (Eqn 1)*

| Matrix code | $k \times 10^2$ | $n$ | $r$ |
|---|---|---|---|
| Matrices loaded with sodium salicylate | | | |
| A1 | 3.7 (0.02) | 0.56 (0.002) | 0.9993 |
| A2 | 4.7 (0.05) | 0.54 (0.003) | 0.9999 |
| B1 | 2.8 (0.07) | 0.61 (0.006) | 0.9998 |
| B2 | 2.6 (0.09) | 0.60 (0.003) | 0.9995 |
| B3 | 2.5 (0.06) | 0.63 (0.006) | 0.9998 |
| C1 | 1.4 (0.05) | 0.70 (0.008) | 0.9996 |
| C2 | 1.7 (0.03) | 0.67 (0.004) | 0.9999 |
| C3 | 1.1 (0.04) | 0.69 (0.007) | 0.9995 |
| C4 | 1.6 (0.04) | 0.65 (0.005) | 0.9998 |
| D1 | 0.6 (0.01) | 0.68 (0.004) | 0.9997 |
| D2 | 0.9 (0.03) | 0.65 (0.006) | 0.9992 |
| D3 | 1.1 (0.03) | 0.67 (0.005) | 0.9996 |
| Materials loaded with theophylline | | | |
| A1 | 1.0 (0.02) | 0.69 (0.005) | 0.9965 |
| A2 | 1.4 (0.02) | 0.69 (0.003) | 0.9994 |
| B2 | 0.6 (0.01) | 0.72 (0.005) | 0.9982 |
| C1 | 0.4 (0.01) | 0.77 (0.004) | 0.9986 |
| D1 | 0.04 (0.001) | 0.97 (0.001) | 0.9900 |

Standard deviation in parenthesis. Codes are defined in Fig. 1.

To clarify the effect of matrix swelling on the release process, the IRR was analysed according to the surface area from which the drugs could be released (swelling area).

The release rate per unit swelling area (IRR/$A$) (Fig. 4b) was the same for both the A2 and A1 matrices. However, the values differed according to the drug (NaS or Theo) at the beginning of the release process and approached the same values towards the end of the experimental period.

The effect of the drug on the release from the uncoated matrices was similar to that from the coated ones. In fact, the IRR/$A$ of the matrices loaded with NaS showed higher values than those loaded with Theo at the beginning and approached the same values at the end of the process, the IRR/$A$ profiles of the matrices loaded with Theo always being closer than those of matrices loaded with NaS (Fig. 5b and d). Only the profiles of IRR/$A$ of the D1 matrices were markedly higher, showing decreasing or constant values according to the drug (NaS or Theo).

## Conclusion

Our working hypothesis to explain the different role of the swelling process on the release is the following.

The selective coating modifies water penetration as a consequence of the modification of the matrix geometry. When matrix swelling occurs before drug release, the drug release is controlled by the swelling process. In this case, the release rate per unit swelling area must be the same irrespective of the matrix geometry. If the drug were released before the swelling of the matrix, the release rate per unit swelling area would be different according to both the matrix geometry and drug solubility.

According to the above rationale, the difference of the IRR/$A$ of either NaS or Theo from the matrices with the same modified geometry might be related to the different drug solubility. Instead, the same IRR/$A$ of the drugs from the matrices with different geometry might be a consequence of the effect of the matrix swelling. In our opinion, the IRR/$A$ profiles of NaS from different matrices provide evidence of the effect of the different geometry, i.e., of the position of the uncoated surfaces from which water can penetrate. In contrast, the same release of Theo for unit swelling area would be indicative of release modified by the matrix swelling.

As the IRR/$A$ of both drugs approached the same values only at the end of the process, it can be concluded that the drug solubility predominates over the matrix swelling at the beginning of the release process, whereas the matrix swelling modifies the last part of the release process.

The release from the D1 matrix could be the effect of matrix geometry. In fact, the water penetration from the surface of the interior hole should prevent the decrease in the releasing area of the drug as the diffusion path length increases. The D1 matrix swelled following pseudo-zero order kinetics regardless of the drug (Vandelli and Cameroni, 1993), however, only Theo showed a

constant release. In our opinion, NaS is not released from the D1 matrix according to pseudo-zero order kinetics, since the solubility of this drug would prevent the control of the release process by the matrix geometry.

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