Compressed Matrix Core Tablet as a Quick/Slow Dual-Component Delivery System Containing Ibuprofen

Received: October 16, 2006; Final Revision Received: April 16, 2007; Accepted: April 19, 2007; Published: September 21, 2007

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ABSTRACT

The purpose of the present research was to produce a quick/slow biphasic delivery system for ibuprofen. A dual-component tablet made of a sustained release tableted core and an immediate release tableted coat was prepared by direct compression. Both the core and the coat contained a model drug (ibuprofen). The sustained release effect was achieved with a polymer (hydroxypropyl methylcellulose [HPMC] or ethylcellulose) to modulate the release of the drug. The in vitro drug release profile from these tablets showed the desired biphasic release behavior: the ibuprofen contained in the fast releasing component was dissolved within 2 minutes, whereas the drug in the core tablet was released at different times (≈16 or >24 hours), depending on the composition of the matrix tablet. Based on the release kinetic parameters calculated, it can be concluded that the HPMC core was suitable for providing a constant and controlled release (zero order) for a long period of time.

KEYWORDS: Biphasic delivery system, dual-component tablet.

INTRODUCTION

Biphasic delivery systems are designed to release a drug at 2 different rates or in 2 different periods of time: they are either quick/slow or slow/quick. A quick/slow release system provides an initial burst of drug release followed by a constant rate (ideally) of release over a defined period of time. This type of system is used primarily when maximum relief needs to be achieved quickly, and it is followed by a sustained release phase to avoid repeated administration. Suitable candidate drugs for this type of administration include nonsteroidal anti-inflammatory drugs (NSAIDs) and antihypertensive, antihistaminic, and anti-allergic agents.[1]

Generally, conventional controlled dosage forms delay the release of therapeutic systemic levels and do not provide a rapid onset of action. To modify the release of the drug from these systems, the surface area exposed to a fluid can be restricted by the addition of barrier layers to one or both sides of the tablets.[2-4] However, most multilayer systems attempt to achieve a constant release rate from a tablet, not a biphasic release of the drug. When a single constant rate for drug release does not entirely satisfy the therapeutic objective, the quick/slow delivery system may be an interesting alternative. This biphasic release system can be achieved by the application of an immediate release layer to the conventional layered matrix tablet.[5]

To obtain quick/slow drug release patterns, Uekama et al[6] developed a double-layer tablet that prolonged the release of piretanide for 8 hours; β-cyclodextrin was used in the fast releasing layer, and ethylcellulose (EC) and hydroxypropyl methylcellulose (HPMC) were used in the sustained release layer. Maggi et al[1] considered the same design (compressed double-layer tablet) to achieve a biphasic release of praziquantel and ketoprofen. The quick release layer contained a superdisintegration agent (cross-linked sodium starch glycolate) to increase the drug release rate. The slow release layer consisted of an HPMC matrix tablet. SkyePharma Co has one quick/slow release formulation on the German market: Diclofenac-Ratiopharm Uno 25 mg Quick + 125 mg Slow, which has been produced using the Geomatrix technology (Jago Pharma AG, Muttenz, Switzerland) for multiple-layer tablets. Recently, Li and Zhu,[7] using combinations of versatile minitablets (rapid release, sustained release, pulsatile, and delayed onset sustained with various releasing lag times), obtained a multifunctional and multiple-unit oral drug delivery system, including a quick/slow nifedipine release system.

Another approach to achieving quick/slow drug release involves the use of a compressed core (Figure 1). The core consists of a sustained release tablet, which is coated by compression over the whole surface with a fast-disintegrating formulation. Both the core tablet and the outer powder layer contain a drug. From the viewpoint of manufacturing, this

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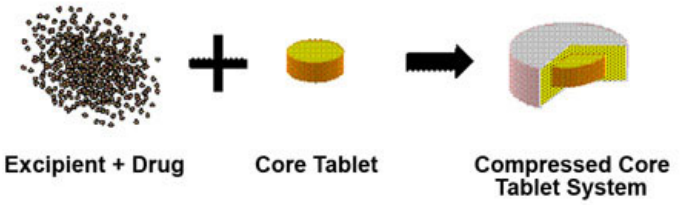

Figure 1. Compressed core tablet system as biphasic delivery system.

technology is an attractive alternative to the production of multilayer dosage forms, because getting additional layers to adhere to the precompressed layers during the double-layer or multilayer tableting process can be difficult. Furthermore, because this system uses conventional manufacturing methods, it is more acceptable to the industry.

Ibuprofen is an NSAID widely prescribed for the treatment of inflammatory pain or rheumatism. Maximum ibuprofen plasma concentrations are achieved 1 to 2 hours after oral administration, but because of the drug's short biological half-life (2 hours),[8] the therapeutic plasma concentration can be maintained only if the ibuprofen is administered frequently. These characteristics make ibuprofen a suitable candidate for administration by a quick/slow delivery system.

In the present study, we aimed to design, prepare, and characterize a quick/slow delivery dosage form as a biphasic tablet in which the coat (outer powder layer) released the drug quickly and the core (central tablet) provided a slow and controlled release of ibuprofen. Proper combination of the quick and sustained release phases would allow the optimization of the fast- and slow-dose fractions as a function of the drug pharmacokinetics and metabolism.[1]

To control the release of the drug (ie, in the prolonged release component of the biphasic system), EC and HPMC were used as sustained release agents in the core tablet. In matrix drug delivery systems, the characteristics of the matrix-forming agent play an important role in the release mechanisms of the drug. Among the hydrophilic polymers, HPMC is one of the carriers most commonly used for the preparation of oral controlled drug delivery systems because of its ability to swell upon gellification once in contact with water. The gel becomes a viscous layer, acting as a protective barrier to both the influx of water and the efflux of the drug in solution.[9,10] On the other hand, inert polymers such as EC can serve as alternatives to the swelling polymers by forming inert matrices, with no physiological action, stable at different pH values and moisture levels, that control the diffusion of the drug toward the surface of the matrix prior to release.

The major objectives of this study were (1) to develop and evaluate a compressed core tablet system, to achieve a quick/slow release of the drug; (2) to study the influence of the type of matrix core on the in vitro performance; (3) to obtain a slow drug release period at a constant rate (zero-order kinetics); and (4) to evaluate the combined effect of a fast release coat together with a controlled release core.

Materials and Methods

Materials

Ibuprofen, a slightly soluble drug (supplied by Laboratórios Medinfar, Lisboa, Portugal) was incorporated in both components of the biphasic delivery system. For the preparation of the controlled release component (core tablet), EC (Ethocel, Fluka Biochemika, Steinheim, Germany) and HPMC (Methocel K100M, Colorcon, Orpington, UK) were considered, whereas for the fast release component, microcrystalline cellulose (Avicel PH 102, FMC Corp, Philadelphia, PA) and sodium croscarmellose (Ac-Di-Sol, FMC Corporation) were used.

Preparation of Dual-Component Delivery System

The dual-component delivery system was prepared by compressing a smaller tablet, forming a central core, with a powder mixture to produce a bigger tablet (Figure 1).

Slow Release Component (Core Tablet)

The core tablets were prepared from binary mixtures of ibuprofen and a matrix-controlling agent (HPMC or EC) by direct compression. EC was milled (electric mill, model A10, IKA, Staufen, Germany) before use. All materials were sieved, and only particles below 63 μm were used, to minimize the lag times when coarse particles are used and to prevent changes in tablet properties due to changes in particle size. The formulations contained 50% (wt/wt) of ibuprofen for HPMC K100M tablets and 85% (wt/wt) of ibuprofen for EC tablets. The tablets, weighing 250 mg, were prepared by direct compression with flat-tip punches and dies with a 9-mm diameter. The punches and dies were fit to an instrumented mechanical press machine (LR 50K, Lloyd Instruments, Fareham, UK) that controlled and recorded the force applied (6.5 kN) and the displacement of the upper punch.

In addition to being used for dual-component delivery system preparation, they were used as single units to evaluate the effect of compression on the structure and in vitro dissolution behavior.

Fast Release Component (External Powder Layer)

The powder used to enrobe the core was formulated to obtain a quick release of the drug. The composition of this component was the same for both formulations: it contained ibuprofen, microcrystalline cellulose, and sodium croscarmellose.

Table 1. Composition of the Biphasic Delivery Systems*

Composition (weight/biphasic system)	Formulation (mg) 1	2
Fast release component		
Ibuprofen	200	200
Microcrystalline cellulose	545	545
Sodium croscarmellose	5	5
Prolonged release component		
Ibuprofen	125	212.5
HPMC K100M	125	—
Ethylcellulose	—	37.5

*HPMC indicates hydroxypropyl methylcellulose.

Microcrystalline cellulose (Avicel PH 102) was used because of its good compaction and disintegration properties. Sodium croscarmellose was used as a superdisintegrant to obtain an immediate release of the drug.

Dual-Tablet System

For the preparation of the quick/slow delivery system, the die of the tableting machine was filled manually with the weighed amounts of the fast release component and the core tablet (Table 1) prior to compression. Half of the fast releasing powder was put into the die to make a powder bed, on the center of which a core tablet was placed. Then the other half of the powder was added to cover the core tablet. The formulations differed in the type and concentration of polymer used in the preparation of the core tablet. Compressed core tablet systems were prepared by direct compression, with flat-tip punches and dies with a 13-mm diameter at 5 kN, as mentioned previously for the core tablets.

Physical Characterization of Core Tablets and Compressed Core Tablet System

Core tablets and compressed core tablet systems were characterized for weight variation (analytical balance AE 200, Mettler-Toledo, Greifensee, Switzerland), thickness (electronic digital micrometer, Palmer, Browne and Sharpe, North Kingstown, RI), crushing strength (Erweka, model TBH 28, Heusenstamm, Germany), and friability (Roche-type friabilometer, 25 rpm for 4 minutes, Sotax model F1 friabilator, Basel, Switzerland).

The crushing strength of the compact was determined by compressing the compact diametrically. The radial tensile strength (σ_X) was calculated from the compact crushing strength and thickness according to the Fell and Newton equation[11]:

$$\sigma_X = \frac{2F}{\pi D h} \qquad (1)$$

where σ_X is the tensile strength (MPa), F is the force required to cause failure in tension (N), D is the diameter (mm), and h is the thickness of the compact (mm).

In Vitro Release Testing

The in vitro release tests were performed according to the US Pharmacopeia paddle method at 150 rpm using an automated dissolution apparatus (Sotax model AT7) containing 900 mL of phosphate buffer (pH 7.2) at 37°C ± 0.5°C. To ensure that the release of the drug was effectively controlled by the pharmaceutical system, the formulations tested in this study were submitted to in vitro release tests that would be able to confirm that the low release rate was dependent on the characteristics of only the dosage form and not the dissolution assay. Ibuprofen is characterized by pH-dependent solubility. If the dissolution medium has a low pH, the in vitro release test results could be owing to the low drug release rate or to the low drug solubility in that medium. If the ibuprofen is tested in optimal pH conditions (alkaline medium), which is the worst-case scenario for ibuprofen controlled release dosage forms, the low dissolution during the in vitro test can be attributed only to the control characteristics of the formulation. The drug released was spectrophotometrically quantified online through a UV/Visible spectrophotometer (Jasco, model V-530, Tokyo, Japan) set at 265 nm. The cumulative fraction of the drug released was calculated from the total amount of ibuprofen and plotted as a function of time. Dissolution studies (n = 3) were performed on both compressed core tablet systems and core tablets to investigate the effect of compression on the dissolution behavior.

The dissolution profiles from compressed and noncompressed core tablets were compared using a similarity factor (f_2)[12]:

$$f_2 = 50\log\left\{\left[1 + \frac{1}{n}\sum_{t=1}^{n}(R_t - T_t)^2\right]^{-0.5} \times 100\right\} \qquad (2)$$

where R_t and T_t are the percentage of drug dissolved at each time point for the test and reference products, respectively. The US Food and Drug Administration and the European Agency for the Evaluation of Medicinal Products have suggested that 2 dissolution profiles can be considered similar if f_2 is between 50 and 100.[13,14]

Release Drug Data Modeling

The suitability of several equations that are reported in the literature to identify the mechanisms for the release of ibuprofen[15] was tested with respect to the release data. Some diffusion models (Korsmeyer-Peppas) are expected to be

Table 2. Physical Properties of the Noncompressed Core Tablet*

Core Tablet	Weight (mean ± SD, mg) (n = 20)	Thickness (mean ± SD, mm) (n = 40)	Tensile Strength (mean ± SD, MPa) (n = 10)	Friability (%) (n = 20)
HPMC K100M	251.2 ± 0.8	4.33 ± 0.02	1.33 ± 0.11	0.51
Ethylcellulose	251.2 ± 0.8	4.49 ± 0.01	0.68 ± 0.05	0.52

*SD indicates standard deviation; and HPMC, hydroxypropyl methylcellulose.

valid only up to ~60% cumulative drug released,[16] so the data for analysis were restricted to that range, excluding also the lag time. The data were evaluated according to the following equations:

Zero-order model[17]:

$$M_t = M_0 + K_0 t \quad (3)$$

Higuchi model[18,19]:

$$M_t = M_0 + K_H t^{0.5} \quad (4)$$

Korsmeyer-Peppas model[20,21]:

$$M_t = M_0 + K_k t^n \quad (5)$$

where M_t is the amount of drug dissolved in time t, M_0 is the initial amount of drug, K_0 is the zero-order release constant, K_H is the Higuchi rate constant, K_K is a release constant, and n is the release exponent that characterizes the mechanism of drug release. The magnitude of the exponent n indicates that the release mechanism is Fickian diffusion, case II transport, or anomalous transport. In the present study (cylindrical shape) the limits considered were $n = 0.45$ (indicates a classical Fickian diffusion-controlled drug release) and $n = 0.89$ (indicates a case II relaxational release transport: polymer relaxation controls drug delivery). Values of n between 0.45 and 0.89 can be regarded as indicators of both phenomena (transport corresponding to coupled drug diffusion in the hydrated matrix and polymer relaxation), commonly called anomalous non-Fickian transport. Values of n greater than 0.89 indicate super case II transport, in which a pronounced acceleration in solute release by a film occurs toward the latter stages of release experiments, resulting in a more rapid relaxation-controlled transport.[22]

Results and Discussion

Physical Properties of Core Tablets and Compressed Core Tablet System

Tables 2 and 3 list the physical properties (weight, thickness, tensile strength, and friability) of the core tablets and compressed core tablet systems, respectively. Both the noncompressed and the compressed core tablets were produced with small weight variations (coefficient of variation <5%) and uniform thickness. Conventional compressed tablets that lose less than 1% of their weight are generally considered acceptable. In the present study, the friability was 1.28% and 1.12% for compressed HPMC and EC core tablet systems, respectively. In a recent study, Waterman and Fergione[23] demonstrated that difficulties in achieving good friability values after press-coating immediate release powder onto controlled release coated tablets result from poor adhesion to the coatings because of their poor compressibility. To solve the poor adhesion problem, a novel adhesive coating (Eudragit RL, polyethylene glycol, and triethylcitrate at a ratio of 5:3:1.2) was proposed,[23] which provided good adhesion between the 2 components reflected on a tablet with low friability.

The composition of the fast component should provide a hard and rapidly disintegrating tablet at low compression forces, and the compaction of the core tablet should not affect the structure or the release behavior of these units. It follows that compaction should not cause the core tablet to develop into a nondisintegrating matrix. Upon evaluation of the crushing strength, visual inspection of the fractured surfaces of the dual-component system revealed that the appearance of the core tablet in the compact system was similar

Table 3. Physical Properties of the Compressed Core Tablet Systems*

Formulation	Type of Core Tablet	Weight (mean ± SD, mg) (n = 20)	Thickness (mean ± SD, mm) (n = 20)	Tensile Strength (mean ± SD, MPa) (n = 5)	Friability (%) (n = 10)
1	HPMC K100M	1012.0 ± 3.5	7.34 ± 0.01	0.65 ± 0.02	1.28
2	Ethylcellulose	1014.9 ± 1.7	7.07 ± 0.01	1.13 ± 0.10	1.12

*SD indicates standard deviation; and HPMC indicates hydroxypropyl methylcellulose.

Figure 2. Equatorial fracture showing the surfaces of the compressed ethylcellulose core tablet system.

to that of the original (noncompressed core tablet). This lack of fragmentation or damage demonstrated that tablet cores were prone to keeping their integrity when compacted and remained as coherent individual units after the process of tableting (Figure 2). Thus, during the axial compression in the die, although the core tablet was stressed from several directions simultaneously, it resisted the compression force applied (5 kN).

In studies of compression behavior and pellet and granule compactability, Johansson et al[24-26] and Tunón et al[27] suggested that the degree of pellet deformation was controlled by their porosity before compression, rather than by their ability to withstand an applied force as individual pellets. Deformation of a pellet during compression is probably caused by the repositioning of the primary particles that constitute the pellet. Because of how these tablets are produced, low porosity is to be expected for these cores. In this case, the possibility for the primary particles to have sufficient freedom to move when the tablets are stressed is limited, and the degree of deformation that the tablets undergo during compression is low. Furthermore, at low porosities, the primary particles might be rigidly positioned alongside each other, which can also make it difficult for particles to change positions.

Dissolution Testing of Compressed Core Tablet System

Figure 3 shows the release profiles of ibuprofen from the bicomponent delivery systems. Figure 4 shows the contributions of each component (fast/prolonged) to the release profiles of ibuprofen from compressed core tablet systems containing either an HPMC or an EC core as a prolonged release component. According to these figures, the release profiles are characterized by a burst release within a few minutes (less than 2 minutes, Figure 3), followed by a slow release period, typical of a biphasic quick/slow delivery system. For both formulations, upon contact with the dissolution media, the large tablets rapidly disintegrated into the fast-releasing phase (containing 200 mg of ibuprofen) and the matrix core tablet (HPMC or EC). The prompt tablet disintegration was due to the presence of sodium croscarmellose, which swells very quickly when in contact with water. After the initial phase, the release was dependent on the composition of the matrix core, in particular, the type and concentration of the polymer. The core tablet kept the ibuprofen release slow for more than 24 hours (HPMC core) or almost 16 hours (EC core). The ability of the HPMC particles to hydrate and form a gel layer around a core is well known and is essential to sustaining and controlling the release of a drug from a matrix.[9] Throughout the dissolution test, a continuous gel layer formed in the HPMC matrix core was responsible for shaping the release of the drug. After 24 hours of dissolution testing, it was evident that the gel layer around the HPMC cores and the EC cores had kept its integrity, exhibiting a porous structure when observed in an optical microscope. Using a different technology, compressed minitablets systems, Lopes et al[28] also obtained a quick/slow ibuprofen release. The fast release component was similar in both studies, but the slow release component in the Lopes et al study consisted of minitablets instead of a single core tablet. The composition of the minitablets was the same as that of the core tablets. In the case of compressed minitablets, these multiparticulates units, upon dispersion in the dissolution media (less than 2 minutes), controlled the release of ibuprofen at a slow rate for almost 8 hours. The minitablets provide a larger surface area, resulting in a faster release of ibuprofen when compared with the release of the drug from a single tablet core.

In the release of the drug from the core tablets, different dissolution profiles (HPMC or EC) were observed. From the

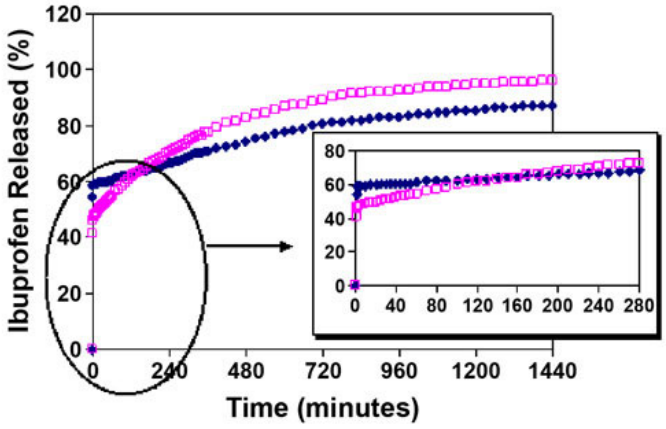

Figure 3. In vitro ibuprofen release profiles from biphasic systems:, compressed hydroxypropyl methylcellulose core tablet;, compressed ethylcellulose core tablet.

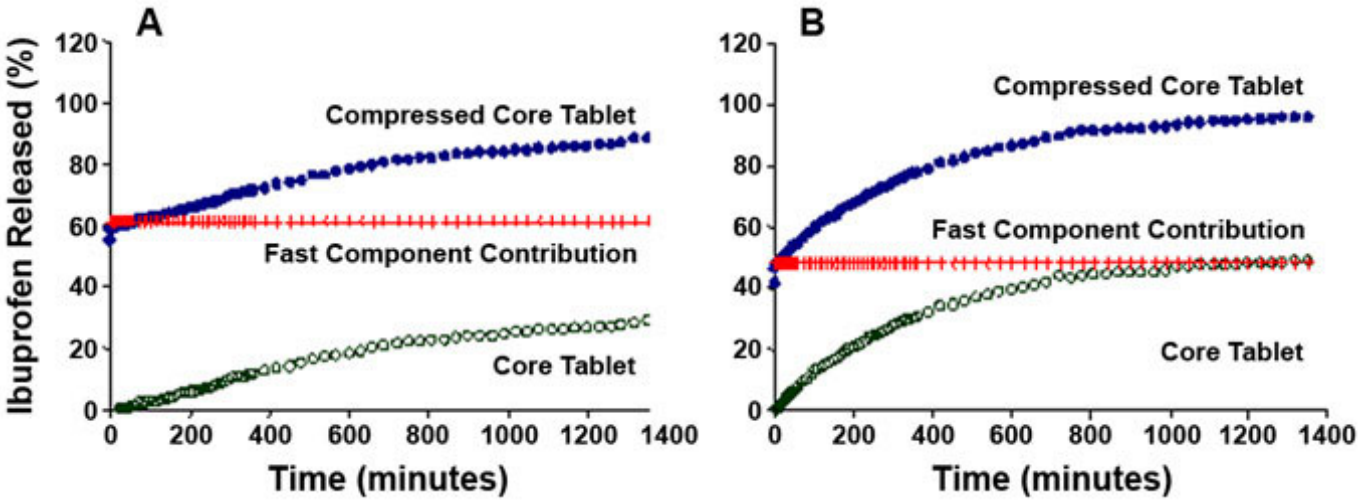

Figure 4. In vitro ibuprofen release profiles from compressed core tablet systems, fast component and core tablet contribution: (a) compressed hydroxypropyl methylcellulose core tablet system, (b) compressed ethylcellulose core tablet system.

plots (Figure 4) it can be seen that the release rates are affected by the composition of the core present in the biphasic system.

To perform a comparative study, double-layer tablets that used the same composition for the fast and prolonged components were designed. The adherence of the second layer to the precompressed layer was a major problem, and the results from this test were discarded. However, it must be pointed out that double-layer tablets were proposed by Uekama et al[6] and Maggi et al[1] to produce a quick/slow profile release of a drug. In the biphasic delivery system developed by Maggi et al,[1] the in vitro dissolution tests showed that the drugs (ketoprofen and praziquantel) contained in the fast release layer dissolved within 15 minutes because of the presence of a cross-linked sodium starch glycolate (superdisintegrant), while the drug contained in the HPMC prolonged release layer was released at different times, depending on the percentage and viscosity grade of the HPMC. Maggi et al[1] also demonstrated that a wide range of fairly constant dissolution rates can be obtained for the HPMC layer. In the Uekama et al study,[6] the double-layer tablets provided a typical quick/slow profile release of the piretanide. For a rapidly releasing fraction, hydrophilic beta-cyclodextrin derivates were employed to form a water-soluble complex with piretanide. For a sustained release fraction, cellulose derivate (combination of hydroxypropylcellulose and EC) matrices were used.

Ideally, the release of the drug should not be affected by compaction. The main purpose of compaction of the core tablet is to ensure that it has the same properties (eg, drug release properties) as the original core. Structural changes (ie, deformation) of the core tablet should be minimized, particularly by application of the compaction force, to avoid modification of the drug release.

Figure 5 compares the profiles of the core tablets before and after compaction into dual-component systems for both HPMC and EC. In this figure, the contribution of the ibuprofen in the fast release component was not considered.

Dual-component formulations have shown the ability to release the intact core tablets into a dissolution medium while maintaining a dissolution profile similar to that of the original core, emphasizing their integrity (f_2 = 78 and 77 for noncompressed and compressed HPMC and EC core tablets, respectively) (Figure 5). For the f_2 calculation, the

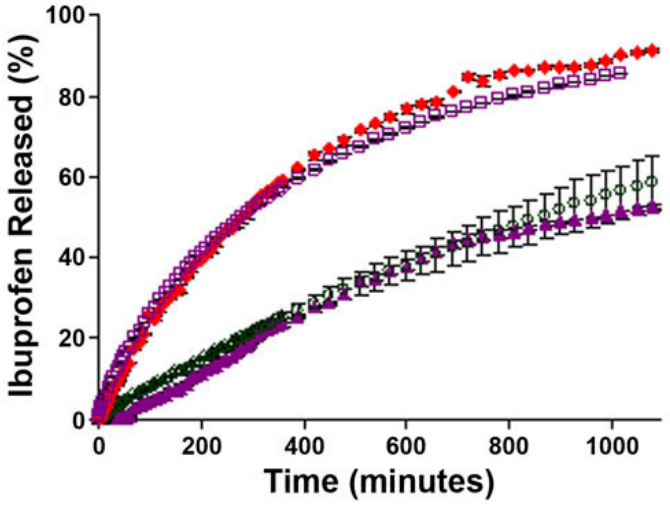

Figure 5. In vitro ibuprofen release profiles from noncompressed HPMC () and EC () core tablets and compressed HPMC () and EC () core tablets (mean ± SD). HPMC indicates hydroxypropyl methylcellulose; EC, ethylcellulose; and SD, standard deviation.

Table 4. Fitting of the Kinetics Model for Tablet Systems*

Tablet System	Type of Polymer in Core Tablet	Zero-Order Equation		Higuchi Equation		Korsmeyer-Peppas Equation		
		K_0	R^2	K_H	R^2	K_K	n	R^2
Core	HPMC	0.0551	0.9890	2.0768	0.9847	0.3464	0.76	0.9992
	Ethylcellulose	0.1532	0.9672	3.3812	0.9960	1.8619	0.59	0.9985
Core + outer layer	HPMC (formulation 1)	0.0270	0.9763	0.9369	0.9670	0.1514	0.76	0.9895
	Ethylcellulose (formulation 2)	0.0847	0.9788	1.8527	0.9911	0.6467	0.67	0.9983

*HPMC indicates hydroxypropyl methylcellulose. K values are release rate constants according to the models considered; R^2 values are determination coefficients; and n is the exponent of the Korsmeyer-Peppas model.

contribution of the ibuprofen in the immediate release component of the compressed core tablet system was subtracted from the total amount of released drug. The maximum SD was 7% for drug release in the EC core. Thus, the structure presented by the core tablets was hard enough (1.33 and 0.68 MPa for HPMC and EC noncompressed core tablets, respectively) to accommodate the force throughout compaction, without major deformation or fracture. A slower release rate was obtained for the noncompressed and compressed HPMC core tablets than for the EC core tablets.

Drug Released From Compressed Core Tablet System

The results for the fitting of the kinetics model for drug release from noncompacted and compacted core tablets are shown in Table 4. The values for the release rate constants (K_0, K_H, K_K), the correlation coefficients (R^2), and the release exponent (n) are considered. The correlation coefficient (R^2) was used as an indication of the best fit, for each of the models considered.

Some release mechanisms can be better elucidated indirectly, either by comparing the fitting of the models of relaxational polymer and matrix erosion (Equation 3) and of pure diffusion (Equation 4), or by the exponent n (Equation 5). For the compressed HPMC core tablet system, the model that best fit the data was the zero-order model (Equation 3, R^2 = 0.9763), when compared with the Higuchi model (Equation 4, R^2 = 0.9670). The n value for this system was 0.76, which meant that the n value and the comparison of model fitting led to the same conclusion: the mechanism of release for the core with HPMC can be described as case II transport. Thus, during the dissolution test, the HPMC core was subjected to 2 simultaneous processes, the formation of a gel layer and its progressive erosion. Although matrix erosion is generally influenced by the hydrodynamic conditions, in this case, the synchronization of the 2 processes led to a nearly constant release rate. It can be concluded that relaxation of the polymeric chain and erosion of the matrix were very important in controlling the release rate of the drug from the HPMC core tablets. Regarding the results for the noncompressed HPMC cores (R^2 slightly higher for the zero-order model, 0.9890, than for the Higuchi model, 0.9847, and n = 0.76), similar conclusions can be obtained for the release mechanism. This is confirmed by a similar in vitro ibuprofen release profile obtained from the contribution of the core tablet in the release of the dual-component system and of noncompressed core tablets, based on the f_2 values (Figure 5).

In the case of the EC core tablet system, the best fit was obtained when the Higuchi model was applied (Equation 4, R^2 = 0.9911). Taking also into account the n value, 0.67, we can say that the mechanism controlling the release is anomalous diffusion. Similar conclusions can be obtained for the original EC core (Equation 3, R^2 = 0.9960 and n = 0.59). In these cases, both results also suggest that the release of the ibuprofen occurred by a combination of both mechanisms, diffusion of the drug through the matrices in the EC tablets and matrix erosion.

However, the analysis of the results applying these mathematical models is purely empirical, and no definitive conclusion can be drawn concerning the dominant mass transport mechanisms.

CONCLUSIONS

A dual-component oral delivery system was achieved by a quick/slow delivery system, characterized by an initial rapid release phase, corresponding to the drug present in the external layer, followed by a period of slow release, corresponding to the drug from the central core tablet. The 2 different release phases can be easily adjusted in both delivery rate and ratio of the dose fractions (immediate/slow), according to the pharmacokinetics and therapeutic needs, to provide the desired in vivo profile. The results obtained with the dissolution test show that the release profile is dependent on both the type and amount of polymer in the core tablet. After the disintegration of the biphasic system, both types of polymers (HPMC and EC) were able to modulate the release of the ibuprofen for a prolonged time (>24 hours or almost 16 hours, respectively) with a dissolution profile similar to that of the

nontableted matrix tablets, based on the f_2 values, suggesting their integrity after compaction.

ACKNOWLEDGMENTS

The authors are thankful to Laboratórios Medinfar (Lisboa, Portugal) for the gift sample of ibuprofen. This work was supported by Fundação para a Ciência Tecnologia and Programa Operacional Ciência a Inovação 2010 program (Fundo Social Europeu) doctoral grant (SFRH/BD/7002/2001).

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