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Gastroretentive drug delivery systems with L-dopa based on carrageenans and hydroxypropylmethylcellulose

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ABSTRACT

A comprehensive study was conducted to investigate the effects of carrageenans, and hydroxypropylmethylcellulose (HPMC) on the properties of hydrodynamically balanced systems (HBS) containing L-dopa as a model drug. The novel integrated approach included measurements of: solvent uptake, erosion, apparent density and changes in the internal structure of dosage forms during dissolution test by means of a USP4 compatible MRI. Differences in water ingress into the matrices with pure carrageenans (ι, κ, λ) or low viscous HPMC, were detected by non-invasive magnetic resonance imaging. Matrices based on carrageenans subjected to rapid hydration and erosion, were not able to maintain satisfactory floating properties for a sufficiently long period of time. The application of carrageenans in mixtures with HMC promoted water uptake by HBS formulations. The effect produced by varying the polymer blend's composition on release of the L-dopa was also studied. Dissolution data was fitted to Korsmeyer–Peppas equation. For matrices containing mixtures of carrageenan and HPMC, the linear increase in the releasing rate constant, *K*, with the carrageenan content in the matrix was observed.

1. Introduction

Orally administered, controlled drug delivery is both the most convenient and therapeutically beneficial therefore, it is a common drug administration method. However, certain drugs cannot be delivered in a traditional controlled release manner. These include active substances, which: (1) are acting locally in the stomach, (2) have a narrow absorption window in the upper part of gastrointestinal tract, (3) are degradable in the intestinal environment, or (4) exhibit low solubility at intestinal pH.

Various approaches have been made to increase the gastric retention time of a dosage form (Streubel et al., 2006). The illustrative examples of gastro-retentive drug delivery systems with drug release that is localized in the stomach are hydrodynamically balanced systems (HBS) (Arora et al., 2005; Bardonnet et al., 2006; Ali et al., 2007). HBS swells upon contact with gastric fluid, and the gel layer formed on HBS's surface ensures its floating properties and controlled release. The key element in the development of gastro-retentive dosage form is an appropriate selection of hydrophilic polymer, which provides adequate flotation characteristics and release of the drug substance. Our previous experience with HBS formulations (based on hydroxypropylmethylcellulose (HPMC)) demonstrates that application of polymers with various physico-chemical properties may provide formulations with similar dissolution capacities (Dorożyński et al., 2010).

In order to improve HBS's functionality, we used carrageenans and their mixtures with HPMC. Carrageenans are high molecular weight sulfated polysaccharides that are extracted from marine red algae *Chondrus crispus* or *Gigartina stellata* belonging to *Rhodophyceae* class. From the functional point of view, three main carrageenan forms exist: lambda, kappa and iota. Structural differences of specified carrageenan types relate to their different gel formation and water uptake properties. For example, the lambda type (λ-carrageenan) forms viscous solutions, while iota (ι-carrageenan) and kappa (κ-carrageenan) form hydrogels in contact with water characterized by different rigidities (Campo et al., 2009). There is a great potential for commercially available carrageenans, in the preparation of controlled release matrix systems, due to their gelling and viscosity building properties (Bonferoni et al., 1994, 1998, 2000; Gupta et al., 2001; Nerurkar et al., 2005). Carrageenans have been also used as gel forming agents for formulation of controlled release systems. The matrix systems based on λ-carrageenan and HPMC mixtures, are characterized by pH-independent drug release profiles lasting about 24 h (Bonferoni et al., 1998). However, it was demonstrated that the erosion of carrageenan matrices is affected by the pH of the dissolution medium, and it is too intensive at acidic environment. It has been also noted, that intensity of the erosion process in dissolution medium with acidic characteristics can be

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further reduced by an addition of slowly erodible polymer, e.g. hydroxypropylmethylcellulose (Nerurkar et al., 2005).

Drug dissolution from hydrophilic matrix systems is associated with water ingress into the matrices. During dissolution, several physicochemical phenomena occur simultaneously (Li et al., 2008). The intensive research that elucidates the mechanisms of drug release from polymeric matrix systems has been carried out through last decades (Colombo et al., 1995; Pillay and Fassihi, 2000; Bettini et al., 2001) however, in most of these studies, HPMC has been used as a model of polymeric matrix. Hence the knowledge of hydration phenomena in such systems is relatively wide. The systems consisting of other polymeric substances, especially naturally abundant, have been rarely employed in such analyzes. Carrageenans are representatives of polyanionic polymers, which should behave in contact with dissolution medium in different manner than HPMC.

In recent years, magnetic resonance imaging (MRI) has been used to study hydration phenomenon in pharmaceutical products containing hydrophilic polymer matrices. MRI is one of the most promising techniques, which provides the opportunity for non-destructive recording of spatial distribution of certain nuclei e.g. protons, in the sample. Since measured MRI signal intensity is proportional to water content of the sample, visualization of dosage form during hydration is possible. Moreover, MRI does not influence or alter the processes of diffusion, swelling or erosion of the dosage form (Fyfe et al., 2000; Baumgartner et al., 2005; Kulinowski et al., 2008).

In this study we present a comprehensive analysis of the carrageenan containing HBS formulations. The measurements of solvent uptake, erosion and apparent density were performed. Changes in the internal structure of dosage forms during dissolution test were measured using USP4 compatible MRI. The specific objectives of this work included investigation of the suitability of carrageenans with different substitution types and their mixtures with low viscosity grade HPMC for the preparation of hydrodynamically balanced systems. The relationship between kinetics of drug release and the type and amount of carrageenan included in the matrix was also assessed.

2. Materials and methods

2.1. Materials

Model drug: L-dopa (LD) was purchased from Sigma–Aldrich. Excipients: Gelcarin GP379 – carrageenan ι (CI), Gelcarin GP812 – carrageenan κ (CK), Viscarin – carrageenan λ (CL), were gifts from FMC BioPolymer, HPMC Metolose 65 SH 400 was a gift from Shin-Etsu, Japan, white opaque hard gelatin capsules, Coni-Snap size 1 were obtained from Capsugel, Bornem, Belgium. All other materials were of analytical grade.

2.2. Formulations

The formulations, as described in Table 1, were prepared in mortar and capsules were filled manually with non-compressed powder mixtures corresponding to 100 mg of drug. The simplicity of chosen HBS formulations allows for observations of interactions between drug and polymer, not disturbed by presence of additional excipients e.g. lubricants, fillers, binders. The capsular form of HBS ensures avoidance of additional technological manipulations e.g. granulation, tableting which can alter properties of the formulations.

2.3. MR imaging and dissolution study

We used, as previously described, experimental methods for simultaneous dissolution and MRI experiments (Dorożyński et al., 2007; Kulinowski et al., 2008). Briefly, for MRI measurements, we used a 4.7 T horizontal super-conducting magnet (Bruker, Germany). The MR console MARAN DRX (Resonance Instruments, Great Britain) was interfaced with the magnet. A MR-compatible flow-through cell system was made of Plexiglas® and combined with an MR, rf probe, for MR signal detection which was simultaneous with dissolution of the drug. The circulation of the solution was obtained by using a piston pump (HKP 60 Erweka GmbH, Germany). The experiments were carried out in 0.1 M HCl solution and the following parameters of dissolution study were applied: the total volume of solution was 1000 ml; the circulation of medium was maintained in the closed loop at 37 °C with the flow rate of 40 ml/min. The experiment was carried out for 300 min or up to disintegration of the dosage form.

A flow compensated spin-echo MR sequence was used to record the HBS evolution during dissolution studies. The imaging sequence parameters were as follows: echo time (TE) of 19 ms, repetition time (TR) of 625 ms, number of excitations (NEX) of 4. Matrix size of 256 × 256 for the 3.5 cm field of view (FOV) was used and the slice thickness was 1 mm, resulting in spatial resolution of 0.14 mm × 0.14 mm × 1 mm. Total imaging time to formulate a 3D image was approximately 10 min. The images were acquired every 15 min.

For dissolution study, the samples of solution (5 ml) were withdrawn every 15 min. Equal amounts of dissolution media were replaced immediately after sample's withdrawal. Concentration of released LD was determined by measuring the UV absorption at 280 nm. Evaluation of the released amount of the drug was made using calibration curve. Dissolution experiments were performed in triplicate.

2.4. Dissolution data treatment

Modeling of dissolution data was performed using "Kinet_DS" software (http://sourceforge.net/projects/kinetds/files/), which enables simultaneous analysis of many dissolution profiles and application of various kinetic and empirical models (Korsmeyer–Peppas, Hixson–Crowell, Higuchi, zero, 1st, 2nd and 3rd order kinetic etc.).

After initial suitability analysis of several models, Korsmeyer–Peppas model was chosen as the most suitable and robust approach. The model is described by Eq. (1).

$$\frac{Q_t}{Q_\infty} = Kt^N \quad (1)$$

where Q_t – amount of LD released at time t, Q_∞ – amount of drug released in the infinity [%], N – release exponent, and K – release constant.

2.5. Image analysis

Images were reconstructed from multi-dimensional MR raw-data (RImage files native MARAN DRX format) with two-dimensional digital Fourier transformation. The pixel intensity in the images was proportional to proton concentration weighted by relaxation times $T1$ and $T2$. The black and dark grey colors (values near zero level) represented "dry" regions of the HBS. The higher values corresponded to increasing water concentration in partially and fully hydrated parts of the dosage forms.

The image analysis was performed using ImageJ 1.43u software for Mac Os X (NIH, Bethesda, MD, USA). In the first step, images with cross-section of central region of the HBS were chosen. Then, the regions of interest (ROI) containing HBS were selected. In the next step, the histograms of signal intensities in ROIs were made. Based on the information from histograms, the thresholds were determined. These thresholds were used to separate the

Table 1
Composition of formulations used in the study (mg per capsule).

Formulation	Substance				
	LD	HPMC Metolose 65SH 400cP	CI Carageenan ι Gelcarin GP379	CK Carageenan κ Gelcarin GP812	CL Carageenan λ Viscarin
C-0	100	100	–	–	–
CI-100	100	–	100	–	–
CI-80	100	20	80	–	–
CI-60	100	40	60	–	–
CI-40	100	60	40	–	–
CI-20	100	80	20	–	–
CK-100	100	–	–	100	–
CK-80	100	20	–	80	–
CK-60	100	40	–	60	–
CK-40	100	60	–	40	–
CK-20	100	80	–	20	–
CL-100	100	–	–	–	100
CL-80	100	20	–	–	80
CL-60	100	40	–	–	60
CL-40	100	60	–	–	40
CL-20	100	80	–	–	20

areas in the image with specific intensity characteristics. After thresholding-based segmentation the areas of segmented regions were measured, i.e.: total area of HBS cross-section, dry core of HBS. The boundaries of the regions were detected using Sobel edge detector filter.

HBS size and shape were measured and quantified using Feret's diameter, the perimeter and the circularity. Feret's diameter was evaluated as the longest distance between any two points along the selection boundary. The perimeter was defined as a length of the outside boundary in the selection. The circularity was calculated using the following equation:

$$C = \frac{4\pi A}{p^2} \quad (2)$$

where C – circularity, A – total HBS area, and p – perimeter.

A C value of 1.0 indicates a perfect circle. As it approaches 0, it indicates an increasingly elongated polygon.

2.6. Water uptake and erosion studies

The hydration of HBS was recorded with gravimetric method. The experiment was carried out in the apparatus 4 (DFZ with HKP 60 Erweka GmbH, Germany). Experimental conditions corresponding with dissolution study conditions were maintained. The samples were removed from the solvent, drained with absorbent tissue and weighted accurately. The samples were then moved onto the Petri dish and dried in oven with circulating air at 80 °C to the constant weight. After storage in desiccator overnight, the dried mass was weighted.

The hydration (H) of the HBS was calculated using Eq. (3).

$$H = \frac{W_t}{W_0} \cdot 100\% \quad (3)$$

where W_t is the weight of wet HBS at time t and W_0 is initial weight of HBS.

The erosion (E) of HBS was calculated using the following formula:

$$E = \frac{W_{dt}}{W_0} \cdot 100\% \quad (4)$$

where W_{dt} is dried HBS weight at time t and W_0 is initial weight of HBS.

2.7. Apparent density and floatation

The apparent densities of HBS formulations were measured using an electronic densimeter EW 200 SG (A&D Japan). The dosage forms were weighted (the result remained in the memory of the apparatus) then placed in the 500 ml (22 °C) of HCl 0.1 M and the density was measured. The floating behavior of prepared HBS was studied during drug dissolution experiments. The floating durations of HBS were determined visually.

3. Results and discussion

3.1. Magnetic resonance imaging of HBS containing L-dopa polymer binary mixtures

3.1.1. Temporal changes of area of HBS

The images recorded every hour during the dissolution studies are presented in Fig. 1, as an example of behavior of the matrices during dissolution. For better visualization of particular areas occurring in swelling HBS, initial preprocessing of the image, based on segmentation and edge detection, was made. The differences between particular formulations are clearly visible. HBS with carrageenan kappa swelled continuously throughout the time of experiment. The floatation of this formulation was ensured by retaining dry core. In cases of systems with other carrageenans,

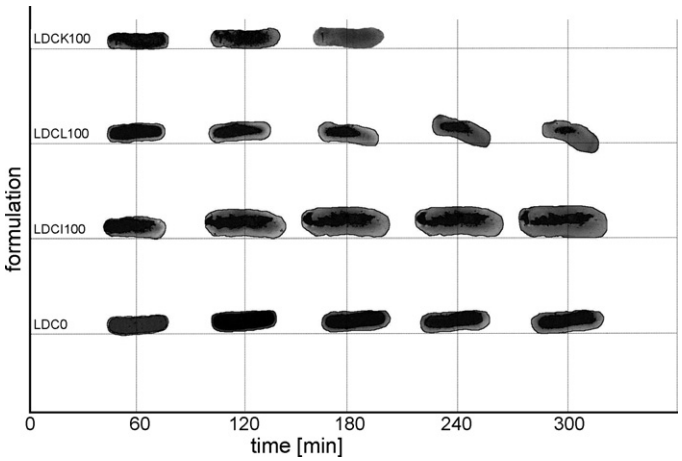

Fig. 1. MR images depicting behavior of HBS during dissolution.

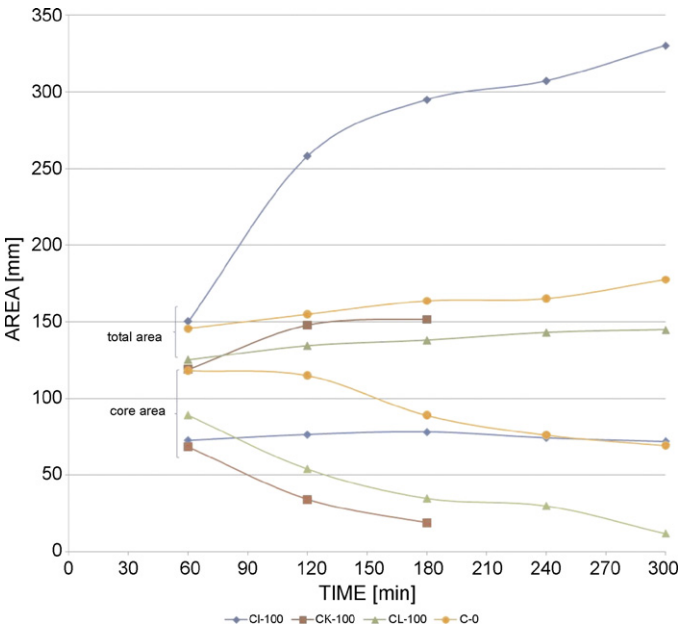

Fig. 2. Time evolution of total area and dry core area of HBS.

water penetration caused decay of dry core and resulted in loss of their floating capabilities. For comparison, in the HBS based on the HPMC, the dry core was only slightly diminished after 300 min.

For quantitative comparison of changes occurring in particular formulations, measurements of total area of the cross-sections and dry cores retained in the HBS were performed. The evolution of areas of HBS is presented in Fig. 2.

Water penetration into the matrix and its interaction with the polymer was dependent upon type of carrageenan. For CK-100, fast ingress of water into the system was observed. The area of the dosage form measured at 60 min was approximately 119 mm^2. At 180 min, a slight increase (up to ~152 mm^2) was observed. The structure of the formulation was retained but the area of the dry core decreased dramatically, from ~57 mm^2 at the beginning of experiment to ~13 mm^2 at 180 min. The dry core was not maintained in the formulation and it sunk immediately after image recording. In contrast, the largest swelling capacity was observed in the case of HBS with carrageenan iota (CI-100). The total area of the cross-section increased from ~150 mm^2 at 60 min to ~330 mm^2 at 300 min. Interestingly, the area of the dry core remained relatively constant during the study. In the beginning, it was ~73 mm^2 while in the end it was 72 mm^2. The intensive swelling of the outer layer caused HBS stretching and deformation of the dry core.

The total area of the system containing carrageenan lambda (CL-100) remained in the range of 125–145 mm^2. The system core decreased gradually from 77 mm^2 to 8 mm^2 in the end of the study. The deformation of the HBS shape due to changes of carrageenan gel rigidity was observed. The investigation carried out by Yuguchi et al. (2003), demonstrated, that the gel formation mechanism depends on the structural characteristics of the polymer. We postulate that in the case of the κ-carrageenan, the gelation took place due to the conformational transition from single chains to double helices and their following association. In contrast, the ι-carrageenan forms cross-linking domains, where double helices are less associated, the λ-carrageenan does not form hydrogel. In the case of HBS containing HPMC as an excipient (C-0), which was used as a reference to carrageenan based formulations, the total area of the system at the beginning was 143.6 mm^2 and slowly increased to 176.1 mm^2. Concurrently, the area of the core decreased from 117.7 mm^2 to 67.4 mm^2. The core in the system was clearly separated from the hydrogel layer.

3.1.2. Geometrical changes of the matrices

The geometrical changes of the HBS observed during the study were assessed using following descriptors: the perimeter, Feret's diameter and the circularity. The temporal changes of the geometrical parameters at 60, 180 and 300 min are presented in Table 2.

The perimeter describes the length of outer boundary of the systems. During the first 60 min, the perimeters of HBS ranged between 51 mm and 55 mm due to the similar size of each prepared formulations. The swelling of the systems affected with increase of the perimeter values. For the carrageenan based formulations, perimeter increase was most effective during the first 180 min, CI-100 reached 77 mm while CK-100 and CL-100 reached 61 mm and 53 mm, respectively. Subsequently the perimeters of CI-100 and CL-100 kept almost constant values, 78 mm and 54 mm. The perimeter of C-0 with HPMC grew gradually throughout the study from 55 mm to 61 mm.

The increase of Feret's diameter and decrease of the circularity of the systems during the first 180 min of the experiment, indicate that HBS swelling was not uniform. It showed initial elongation of the systems, due to sum up of the swelling along the horizontal axis of the systems. For all analyzed formulation with binary mixtures of polymer and LD, for the first 60 min, Feret's diameters of the HBS were in the range from 21 mm to 23 mm, at 180 min it was between 22 mm and 32 mm. Deformation of the shape of carrageenan formulations was associated with the slight decrease of the Feret's diameter in subsequent measurements.

3.2. Floatation and apparent density of HBS

All developed formulations floated immediately due to their low apparent densities. For all prepared formulations densities were in the range: 0.25–0.40 g/cm^3.

3.3. Drug dissolution studies and release kinetics analysis

The differences in the matrix behavior observed for the carrageenan based formulations reflected the drug dissolution. The fastest release rate of LD occurred for HBS containing carrageenan kappa – at 180 min complete dissolution of the drug was achieved. These matrices were essentially ineffective in maintaining the matrix integrity and controlled LD's release. Drug dissolution profiles for HBS containing carrageenans iota and lambda were similar. At 180 min, about 70% of the drug from both formulations was released. In the subsequent 120 min, drug dissolution was slightly slower from the HBS with carrageenan iota; about 89% of LD was released from CI-100 while from CL-100 about 98%. The dissolution of LD from formulation C-0 containing low viscosity grade HPMC was much slower. Total amount of released drug at 300 min did not exceed 50%.

All HBS matrices tested in the experiment demonstrated increased concentration of HPMC in the matrix which resulted in slower drug dissolution. The dissolution profiles of LD from formulations containing mixtures of carrageenans and HPMC are presented in Figs. 3–5.

The dissolution results were fitted to Korsmeyer–Peppas power law equation. A similar model was applied by Gupta et al. (2001) for modeling of dissolution data for controlled release tablets prepared on the base of carrageenans. The results of LD dissolution studies from HBS in terms of parameters determined from Korsmeyer–Peppas model are summarized in Table 3, for confirmation of the selected model relevance for the LD release profiles description.

In this model, the K coefficient is the apparent release rate constant that involves the structural and geometrical parameters of the dosage form and N is the diffusional release exponent. The magnitude of the release exponent, N, indicates the release

Table 2
The temporal changes of the geometrical parameters at 1, 3 and 5 h.

Formulation	CI-100			CK-100			CL-100			C-0		
Time [min]	60	180	300	60	180	300	60	180	300	60	180	300
Perimeter [mm]	54.13	77.15	77.58	55.44	60.65	–	50.63	53.32	53.90	54.80	58.89	61.34
Feret's diameter [mm]	22.34	31.90	32.19	22.59	26.03	–	21.10	22.23	21.79	23.2	25.02	26.22
Circularity	0.633	0.613	0.709	0.616	0.554	–	0.615	0.594	0.625	0.601	0.589	0.588

Perimeter – the length of the outside boundary of the selection.
Feret's diameter – the longest distance between any two points along the selection boundary.
Circularity – a value of 1.0 indicates a perfect circle, as the value approaches 0.0, it indicates an increasingly elongated polygon.

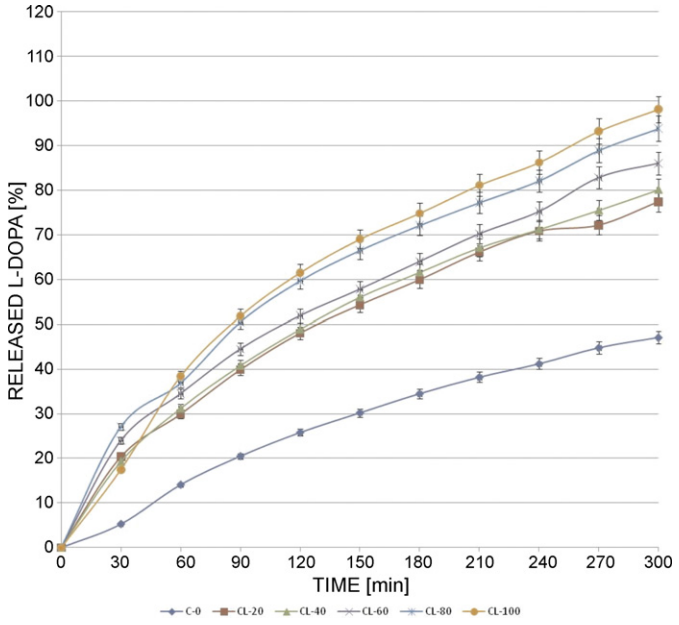

Fig. 3. Release of L-dopa from HBS formulations containing mixtures of carrageenan iota and HPMC. Bars represent the standard deviation.

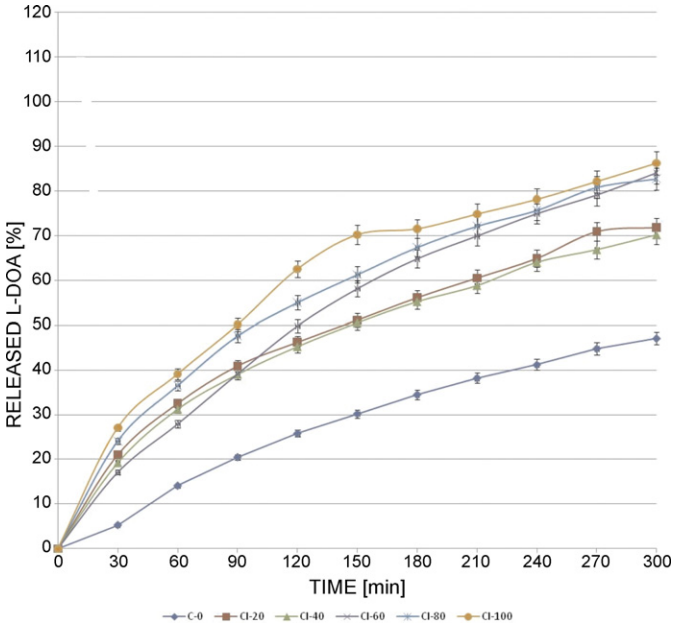

Fig. 5. Release of L-dopa from HBS formulations containing mixtures of carrageenan lambda and HPMC. Bars represent the standard deviation.

mechanism (i.e., Fickian diffusion, case II transport, or anomalous transport). According to the cylindrical geometry of the HBS formulations, in the present study, the limits considered were $N = 0.45$ (indicates a classical Fickian diffusion-controlled drug release) and $N = 0.89$ (indicates a case II relaxation release transport) (Costa and Sousa Lobo, 2001). The values of N between 0.45 and 0.89 can be regarded as an indicator of intermediate condition (drug diffusion in the hydrated matrix and the polymer relaxation) commonly called anomalous transport. The comparison of values of exponent N showed that in the case of formulation C-0 the mechanism of anomalous transport occurred. Introduction of carrageenan into the formulation shifted the values of exponent N above 0.89, indicating that the dissolution mechanism was altered. In the present study, the values of K for particular formulations increased gradually with the concentration of carrageenan in dosage form.

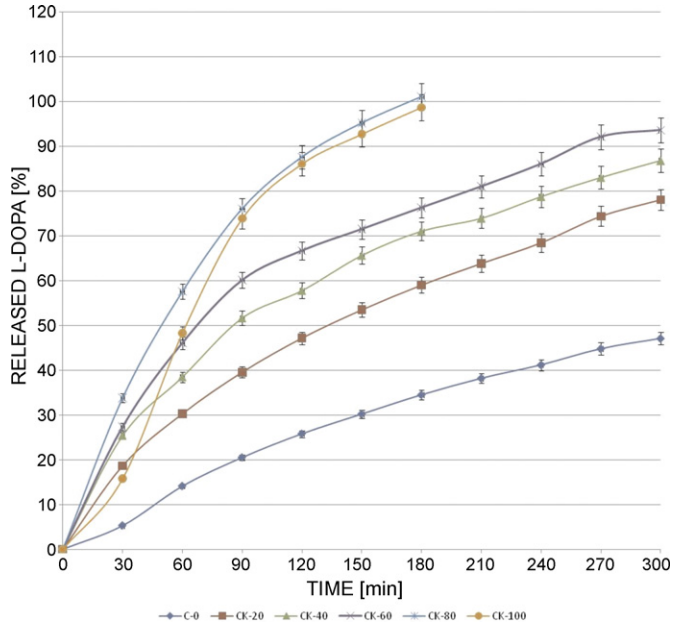

Fig. 4. Release of L-dopa from HBS formulations containing mixtures of carrageenan kappa and HPMC. Bars represent the standard deviation.

Table 3
Release rates and diffusional constants for the release of L-dopa from HBS.

Formulation	N	K [h^{-1}]	R^2
C-0	0.8808	0.3316	0.9982
CI-100	0.9238	0.6014	0.9987
CI-80	0.9276	0.5827	0.9980
CI-60	0.9297	0.5368	0.9993
CI-40	0.9156	0.5298	0.9957
CI-20	0.9161	0.5267	0.9947
CK-100	0.9711	0.7607	0.9948
CK-80	0.9774	0.8609	0.9949
CK-60	0.9378	0.6533	0.9980
CK-40	0.9310	0.6082	0.9942
CK-20	0.9200	0.5317	0.9949
CL-100	0.9195	0.6140	0.9970
CL-80	0.9335	0.6075	0.9965
CL-60	0.9319	0.5693	0.9949
CL-40	0.9246	0.5389	0.9954
CL-20	0.9202	0.5130	0.9963

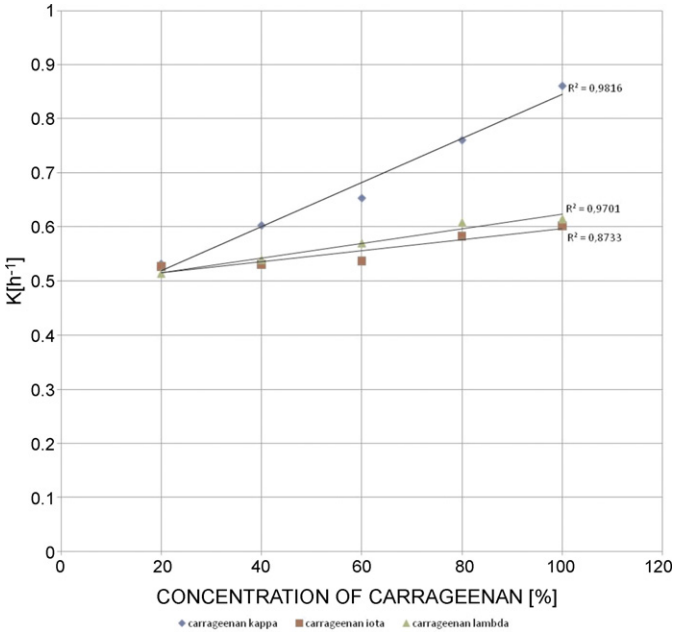

Fig. 6. Relationship between carrageenan content in the polymeric mixture and apparent release rate constant.

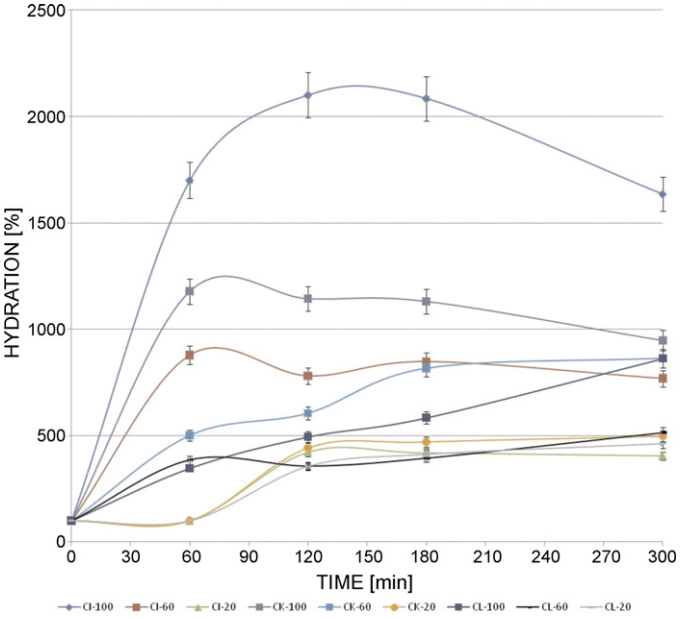

Fig. 7. Results of swelling measurements. Bars represent the standard deviation.

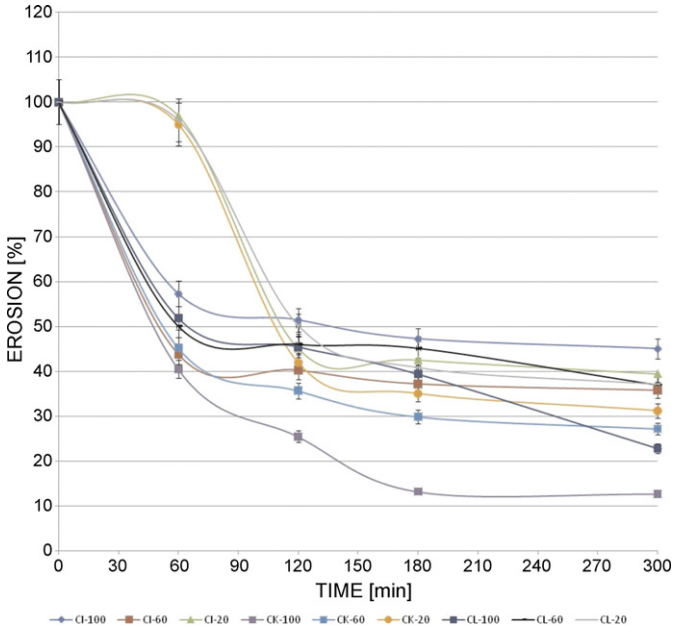

Fig. 8. Results of erosion measurements. Bars represent the standard deviation.

For formulations containing carrageenan iota, *K* values were in the range 0.53–0.60, as for HBS with carrageenans kappa and lambda the ranges of the *K* value were 0.53–0.76 and 0.51–0.61, respectively. For matrices containing a combination of anionic carrageenan and non-ionic HPMC, more control over the release of L-dopa was achieved. The increase in the value of releasing rate constant, *K* was almost linearly related to increasing concentration of the carrageenans (Fig. 6). Formulations with carrageenan kappa were the most sensitive for changes of carrageenan concentration in the matrix while formulations containing carrageenans iota and lambda showed almost similar relation between concentration of carrageenan and *K*.

3.4. Water uptake and erosion

The swelling behavior, of the representative formulations with each carrageenan (CI-20, CK-20 CL-20, CI-60, CK-60 CL-60, CI-80, CK-80 and CL-80), was studied to compare their hydration capacities. The profiles depicting hydration and erosion of HBS are presented in Figs. 7 and 8. Hydration of the polymeric matrix, and the subsequent gel forming on the surface of the HBS and swelling were essential for maintaining the integrity of the dosage form and controlling release of the active substance. During measurements of the HBS systems, rapid surface hydration of the matrices with carrageenans was observed that resulted in its swelling and the consequent formation of a gel layer.

The hydration profiles showed initial increase and subsequent decrease in weight. The highest degree of hydration was achieved for formulations with the highest content of carrageenans. In case of CI-100, the weight of the system at 120 min was 21 times larger than the initial weight of the HBS. For CK-100, the maximum weight of the matrix was almost 12 fold of initial weight. At 300 min, the weights of swollen CI-100 and CK-100 matrices were 16 and 11 times larger, respectively. For formulation CL-100, constant increase in the systems' weight during the experiment was observed. At 300 min the weight of the hydrated system was 8.6 times larger than initial one. The formulations with larger concentrations of HPMC were hydrated to a much lower extent. In parallel with system's swelling, a gradual erosion of the analyzed formulations took place. The systems eroded quickly at 300 min, the weight of dried polymer was 45% of initial weight for CI-100, for CL-100 and CK-100 only 22.8% and 12.7% of initial weight, respectively was retained. The carrageenans promoted penetration of water into the matrix, probably due to the high mobility of the water molecules between polymer chains wherein sulfate groups get hydrated. The improvement in the erosion behavior was noticed along with an increased content of HPMC in the matrix.

4. Conclusions

A novel approach for the evaluation of excipients performance using data obtained by complementary methods was applied. While dissolution study together with hydration/erosion is a common approach, the application of magnetic resonance imaging,

during dissolution study inside the flow-through cell, considerably extends the knowledge about the measured system. The application of MRI provided a unique opportunity to assess the water penetration into the carrageenan-based matrices during drug dissolution. The studies of the behavior of matrix floating systems based on carrageenans, have not been carried out earlier. Particularly, MRI results provided insight into the temporal evolution of matrix regions in terms of overall swelling of the system, gel layer and dry core as well as geometrical parameters (circularity, perimeter).

In this study, we have shown that water penetrates quickly into the matrices of carrageenans. Moreover, carrageenans as additives promote water uptake by polymeric matrices containing mixtures with HPMC because of the high mobility of the water molecules between polymer chains wherein sulfate groups get hydrated. Matrices based on carrageenans alone have limited use for the preparation of floating systems. They are subject to rapid hydration and erosion, and are not able to maintain satisfactory properties for a sufficiently long period of time. The application of mixtures of carrageenans and HPMC increase the flexibility of polymeric excipients applied for HBS formulations. In such formulations carrageenans can modify the properties of polymeric matrices, to obtain tailor-made materials for drug delivery systems.

The practical aspect of this study is, that the presented data can be directly utilized as a starting point (initial selection of excipients) in development of various controlled release carrageenan–HPMC based dosage forms.

Main findings concerning carrageenan–HPMC based matrix systems:

- Linear dependence between dissolution constants and the content of carrageenan in the polymeric matrix.
- The swelling and formation of hydrogel were dependent on the type of the polymer, the highest swelling capacity was observed for the formulations with carrageenan iota.
- Application of mixtures of carrageenans and HPMC, increase flexibility of polymeric excipients applied for HBS formulations. In such formulations carrageenans can modify the properties of polymeric matrices, to obtain tailor-made materials for drug delivery systems.

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