

Dr. Péter Diós

**Preformulation studies and optimization of floating drug
delivery systems based on pharmaceutical technological
and biopharmaceutical parameters**

Design of modified drug delivery systems

Ph.D. Thesis



Supervisor:

Dr. Attila Dévay

University of Pécs, Faculty of Medicine

Institute of Pharmaceutical Technology and Biopharmacy

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1. Introduction

The most frequent application of medicines is the peroral way of administration, which provides easy to take option, relatively low therapeutic cost, various formulations and applicable technologies [1]. Its spread is shown by the fact that more than 50% of commercially available medicines are orally applied preparations [2]. Higher patient compliance may be experienced due to their easy application. Although among the *per os* administered preparations, few are designed with biopharmaceutical aspect meeting with the physiological environment of the dosage forms. While until the 90's not much, however nowadays more frequently modified drug delivery systems are designed containing special excipients and/or manufactured with special technological methods [1]. With novel preparations having controlled release, patient compliance can be increased more, namely multiple daily administrations can be reduced to once a day administration. Another advantage can be a local drug delivery, with which not only the administration of the medicine can be improved, but also the site-specific efficiency of a particular applied active pharmaceutical ingredient (API) may be optimized.

The modification of drug release is performed to achieve a particular therapeutic aim, with which optimized bioavailability of API(s) can be reached by taking the physiological environment into consideration. In the cases of APIs with short elimination half-life, long acting preparations can be designed with the prolongation of API release and absorption. On the other hand, some acute or emergency cases require the possibility of the most rapid effect of the API, which can be developed by the fast API release from preparations.

Modified drug delivery systems (MDDSs) can be classified based on the time and location of drug release. With *per os* administered medicines, the location of drug release in the gastrointestinal tract (GIT) may be in: the mouth, the stomach (e.g. floating, expandable DDSs), the small intestine and/or the colon (e.g. intestinosolvent, enterosolvent, colon targeted DDSs). Thus the location of drug release can be controlled with an appropriate modification of the preparation, and site-controlled systems can be achieved. During drug release in the oral cavity or in the stomach, not only systemic but also local effects may be taken into consideration, while drug release in the small intestine may be expected to cause predominantly systemic effect. In colon-specific therapy, mostly local effects may develop, since absorption is limited/ minimal.

Those modified drug delivery systems, in which the modification is aimed at prolonging the gastric residence time (GRT), are termed gastroretentive drug delivery systems (GRDDS). Via the modification of the time spent in stomach, site- and time-controlled systems may be achieved.

Based on the applied technology, gastroretentive systems can be classified into four separate groups:

- expandable -,
- high density -,
- floating -,
- mucoadhesive preparations.

- 1) Expandable drug delivery systems hinder their transfer through the pylorus with their expansion, swelling via their size without causing gastric obstruction.
- 2) High density drug delivery systems involve formulations of dosage forms having higher average density, than physiological stomach medium. Application of high density ingredients are required to use such as barium sulfate (4.50 g/cm^3), zinc oxide (5.61 g/cm^3) and/or titanium dioxide (4.23 g/cm^3). For significant prolongation of GRT, 2.5 g/cm^3 average density is necessary.
- 3) Floating drug delivery systems (FDDS) are those preparations, which are capable for buoyancy on the surface of gastric medium after a particular time. The mechanism of flotation depends on the applied technology. During flotation, preparations have bulk density lower than the gastric fluid ($\rho < 1.00 \text{ g/cm}^3$) and can remain buoyant without influencing gastric emptying rate. This results in the prolongation of gastric residence time and better control on drug release.
- 4) Mucoadhesive drug delivery systems are capable for bioadhesion onto gastric mucosa resulting in sustaining of GRT, which may cause enhancement of drug absorption in a site-specific manner. Special polymers having mucoadhesive ability are indispensable to apply in these systems, which can adhere to the epithelial surface of the stomach. Mucoadhesion may be an approach, which can be combined with former mentioned technologies in order to achieve not only physically but also chemically resulted gastric retention.

2. Aims

The objective of the dissertation is to summarize the applicability, manufacturing possibilities, excipients and the types of floating drug delivery systems and to optimize a floating, mucoadhesive system aiming at the eradication of *Helicobacter pylori* having desired floating and drug release properties based on preliminary excipient examination. Direct compressed (DC) tablet was chosen as dosage form being a cost-effective technology for pharmaceutical industry requiring fewer procedures.

In order to achieve my goals, the following experimental aims were stated:

- comparison of two types of low substituted hydroxypropyl cellulose (L-HPC 11, L-HPC B1) and their 1:1 mixture based on microscopic, wettability and flowability in order to characterize their role and influence in floating tablets,
- determination of viscosity grade and rheological properties of sodium alginate,
- characterization of parameters related to floating behavior of floating tablets, as well as determination of floating force study parameters,
- evaluation of drug release and floating parameters with variance analysis,
- optimization of floating drug delivery tablets containing metronidazole based on release and floating parameters for better antibacterial effect,
- determination of possible interactions between API and excipients in optimized tablets with differential thermal analysis and isothermal stress tests,
- application of two *ex vivo* mucoadhesive studies in order to determine the mucoadhesive properties of optimized tablets,
- application of X-ray CT imaging technique for *in vivo* tracking of the optimized floating tablets,
- application of high resolution X-Ray CT imaging technique for better view of floating tablets, with which structure of tablets could be assessed,
- application of X-Ray CT imaging of the optimized floating tablet for quantification by Hounsfield unit attenuation and tablet volume,
- recommendation of the optimized composition in order to achieve a more successful gastroretentive therapy.

3. Materials and Methods

Metronidazole (**Fig. 1**) is a nitroimidazole type antimicrobial active substance having potent anti-anaerobic, amebicidal, and antiprotozoal activity. In gastroretentive dosage forms, prolonged contact with the stomach mucosae can be achieved resulting in better local effect against *Helicobacter pylori*.

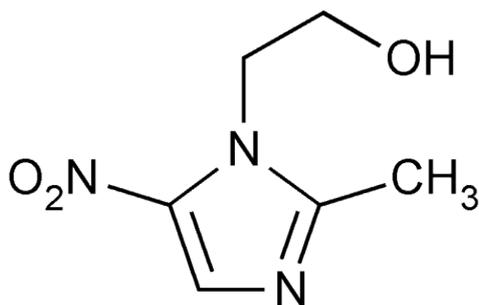


Fig. 1. Chemical structure of metronidazole (1-Hydroxyethyl-2-methyl-5-nitroimidazole; CAS: 443-48-1)

In the experimental sections, the following materials were used:

- sodium alginate,
- low substituted hydroxypropyl cellulose,
- sodium bicarbonate,
- talc,
- magnesium stearate,
- hydrophilic colloidal silicon dioxide,.

In the experimental section of the work, two experimental designs were applied.

- I. The preliminary study focused on the influence of L-HPC 11, B1 and their 1:1 mixture on certain properties of sodium alginate based floating drug delivery systems. In this project, face centered central composite design ($\alpha=1$) was applied with two numerical factors (X_1 , X_2) and with three-levels (+1, 0, -1). One categorical factor was used involving the types of two L-HPCs and 1:1 mixture of L-HPCs. The two numerical independent variables were the sodium alginate (X_1) and particular L-HPC type (X_2). Factors mean the concentrations (%) of the materials in the floating tablets. All tablets contained 150 mg paracetamol and fixed amount of excipients contributing effervescent effect and tablet compressibility. Experimental layout is shown in

Table 1. Dependent variables were the following: floating time, floating lag time, floating force, swelling capability and drug dissolution.

Table 1. Experimental layout of preliminary project

Exp. No.	Sodium alginate, X_1 (%)	L-HPC 11, X_2 (%)	Exp. No.	Sodium alginate, X_1 (%)	L-HPC B1, X_2 (%)	Exp. No.	Sodium alginate, X_1 (%)	L-HPC 11:B1, X_2 (%)
PFS01	0.50	0.50	PFS10	0.50	0.50	PFS19	0.50	0.50
PFS02	35.15	0.50	PFS11	35.15	0.50	PFS20	35.15	0.50
PFS03	0.50	25.00	PFS12	0.50	25.00	PFS21	0.50	25.00
PFS04	35.15	25.00	PFS13	35.15	25.00	PFS22	35.15	25.00
PFS05	0.50	12.75	PFS14	0.50	12.75	PFS23	0.50	12.75
PFS06	35.15	12.75	PFS15	35.15	12.75	PFS24	35.15	12.75
PFS07	17.82	0.50	PFS16	17.82	0.50	PFS25	17.82	0.50
PFS08	17.82	25.00	PFS17	17.82	25.00	PFS26	17.82	25.00
PFS09	17.82	12.75	PFS18	17.82	12.75	PFS27	17.82	12.75

II. For optimization of sodium alginate based floating tablets, face-centered central composite design was used with three factors: sodium alginate (X_1), L-HPC B1 (X_2) and sodium bicarbonate (X_3). Each factor was examined in three levels (+1, 0, -1). Each tablets contained 250 mg metronidazole and constant quantities of excipients contributing effervescent effect and tablet compressibility. Factors mean the concentrations of the materials in the floating tablets. Experimental layout is shown in **Table 2**. Dependent variables were the following: floating lag time, maximal floating force, maximal floating force calculated to 100 mg tablet mass, time needed for maximal floating force and drug dissolution.

Table 2. Experimental layout of optimization project

Exp. No.	Sodium alginate, X_1 (%)	L-HPC B1, X_2 (%)	NaHCO ₃ , X_3 (%)	Total tablet weight (mg)
MF01	5.00	30.00	8.00	463.82
MF02	15.00	30.00	8.00	569.48
MF03	5.00	45.00	8.00	642.67
MF04	15.00	45.00	8.00	865.05
MF05	5.00	30.00	13.00	511.25
MF06	15.00	30.00	13.00	642.67
MF07	5.00	45.00	13.00	737.46
MF08	15.00	45.00	13.00	1046.03
MF09	5.00	37.50	10.50	569.48
MF10	15.00	37.50	10.50	737.46
MF11	10.00	30.00	10.50	538.79
MF12	10.00	45.00	10.50	796.18
MF13	10.00	37.50	8.00	603.86
MF14	10.00	37.50	13.00	686.81
MF15	10.00	37.50	10.50	642.67

The optimization criteria were the following:

- minimization of studies excipients quantities (sodium alginate, L-HPC B1 and sodium bicarbonate),
- improvement of floating parameters: minimization of floating lag time (t_{lag}) and maximization of floating forces (F_{max} and $F_{max/100mg}$),
- minimization of dissolution within the first 30 minutes and its maximization until 6 hours.

4. Results and discussion

4.1. Preliminary studies

The following conclusion could be drawn from the results of preliminary project studies:

- the floating-, swelling behavior and dissolution of the preliminary floating tablets were highly affected by the amount of sodium alginate (X_1) in the compositions,
- L-HPC resulted in rapid disintegration, but this effect could only be manifested, when lower quantity of the matrix former (sodium alginate in 0.5 %) was present,
- when sodium alginate was applied in 17.82 and 35.05 % (**Fig. 2**), then high swelling capability and sustained dissolution (**Fig. 3**) could be observed as well as longer floating lag time and floating time,

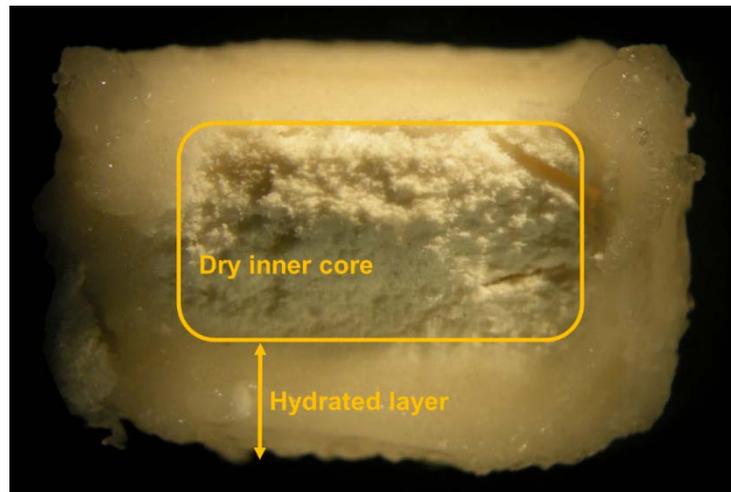


Fig. 2. Macroscopic view of PFS04 floating tablets (sodium alginate: 35.15 %; L-HPC 11: 25.0 %) after 4 hours of hydration

- L-HPC as numerical factor (X_2) was significant in several cases,
- categorical factor (X_3) was only significant at dissolution after 45 min, hence the significance could be identified but the difference was not remarkable, therefore for the further studies L-HPC B1 was used considering its better physical properties (wettability, flowability, bulk and tapped densities),

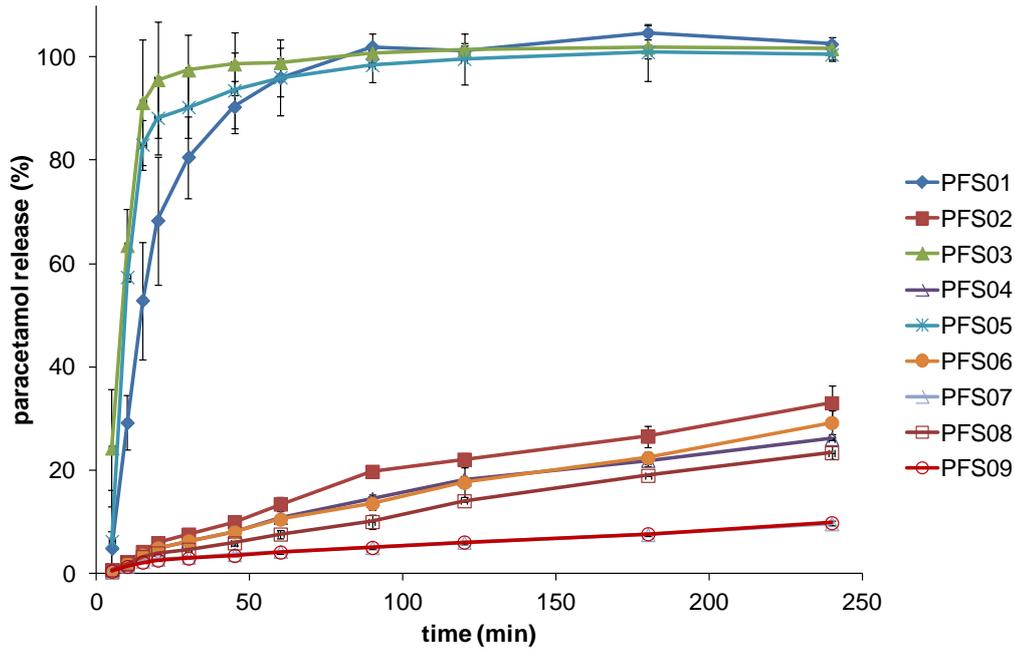


Fig. 3. Dissolution of paracetamol from floating tablets containing L-HPC 11

- floating lag time data indicated that 8 % sodium bicarbonate may have to be increased in order to achieve faster start of buoyancy,
- the range of L-HPC and sodium alginate concentrations was too broad, thus further adjustment in this interval was required in order to create a floating drug delivery systems with desirable floating-, swelling-, dissolution properties.

4.2. Optimization studies

In order to utilize the result of the preliminary project, the optimization project was designed with 5.0-15.0 % sodium alginate (X_1) - and 30.0-45.0 % L-HPC B1 (X_2) concentration. 8.0-13.0 % of sodium bicarbonate was applied as another numeric factor (X_3) in this experimental matrix.

Results of floating lag time studies indicated that rapid buoyancy could be achieved, since t_{lag} of 9 formulations was less than 1 minute. Sodium alginate, L-HPC B1 and the possible interaction of L-HPC B1 and sodium bicarbonate were significant ($p < 0.01$), among which the latter may be explained by the hydration mechanism of the tablets. MF07 showed the shortest floating lag time, which contained the 5.0 % sodium alginate ($X_1: -1$), 45.0 % L-HPC B1 ($X_2: +1$) and 13.0 % sodium bicarbonate ($X_3: +1$). The increase of sodium alginate amount raised floating lag time values, which may be explained by higher coherency of the matrix structure.

Results of floating force studies indicate remarkably high maximal floating forces and maximal floating forces per 100 mg. The maximum was observed at MF07 expressing 26.64 ± 1.18 mN vertical force (26.64 ± 1.18 mN = 2716.52 ± 120.32 mg „resultant weight”).

In vitro dissolution studies of all floating tablets were performed for 6 hours and its result are depicted in **Fig. 4**.

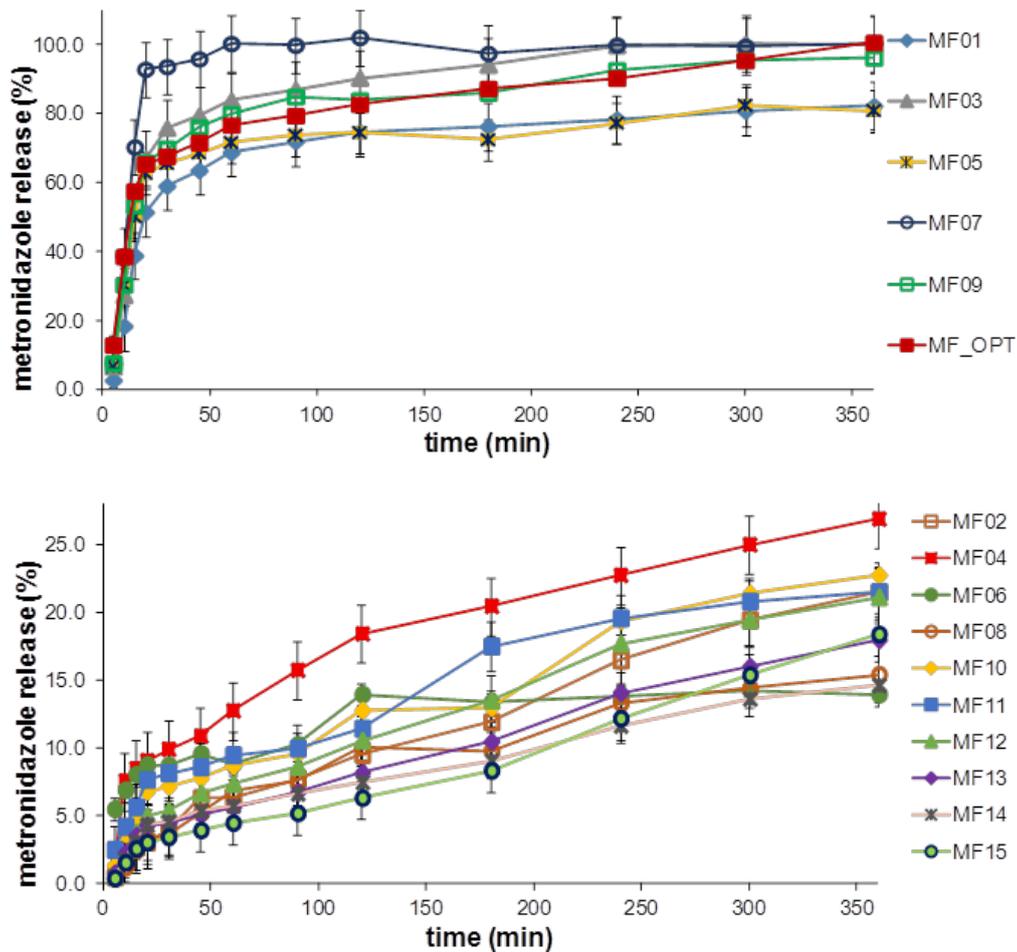


Fig. 4. Dissolution profiles of floating tablets (optimization project)

The most rapid dissolution could be observed at MF07 (sodium alginate: 5.0 %, L-HPC B1: 45.0 %, sodium bicarbonate: 13.0 %) having total dissolution after 60 minutes. Compositions with more than 5.0 % sodium alginate (10.0 or 15.0 %) could not produce more than 26.87 ± 1.05 % metronidazole dissolution after 6 hours. In the case of 5.0 % sodium alginate, the least released amount of metronidazole was circa 80-82 % (MF01, MF05).

Based on the optimization criteria, an optimal composition (MF_OPT) was determined having 5.0 % sodium alginate, 38.63 % L-HPC B1 and 8.45 % sodium bicarbonate by Design Expert 7.0.0 software. Dissolutions of two commercially available non-floating metronidazole

generics were tested, in order to compare them with the optimized formulation. The comparative dissolution is depicted in **Fig. 5**.

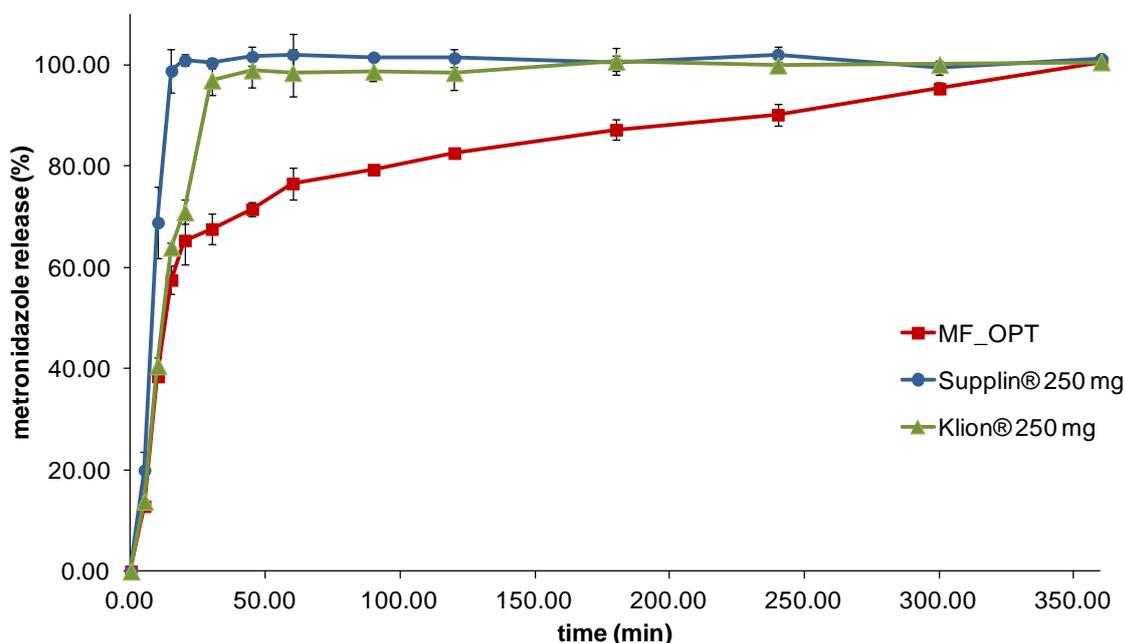


Fig. 5. Comparison of dissolution profiles of two commercially approved non-floating metronidazole tablets and the optimized formulation (MF_OPT)

Results showed that dissolution of MF_OPT could be regarded to be biphasic release involving an initiative rapid - (~60 %) and a prolonged release section (~40 %). MF_OPT tablets had several advantages including a biphasic release and remarkable floating parameters compared to the rapidly released metronidazole from the two approved tablets.

Optimized floating tablets were studied with further tests and evaluations in order to identify their further possibilities and advantages, thus microbiologically detected dissolution -, physical interaction -, *ex vivo* mucoadhesive studies and *in vivo* imaging evaluation were carried out.

Microbiological inhibition of metronidazole released by MF_OPT floating tablets were evaluated in order to show its *in vitro* pharmacological effect as a function of time. Dissolution result of MF_OPT with spectrophotometric detection was compared with the microbiologically detected dissolution (**Fig. 6**). This graph shows a great similarity between assay based on pharmacological effect and UV absorbance assay.

Lower value than 15 at f_1 and value between 50 and 100 at f_2 classified the dissolution profiles to be similar. Difference factor (f_1) 5.23 and similarity factor (f_2) 66.61 were found to be

statistically significant endorsed by Food and Drug Administration, which showed similar dissolution profiles of spectrophotometric and microbiological detection methods.

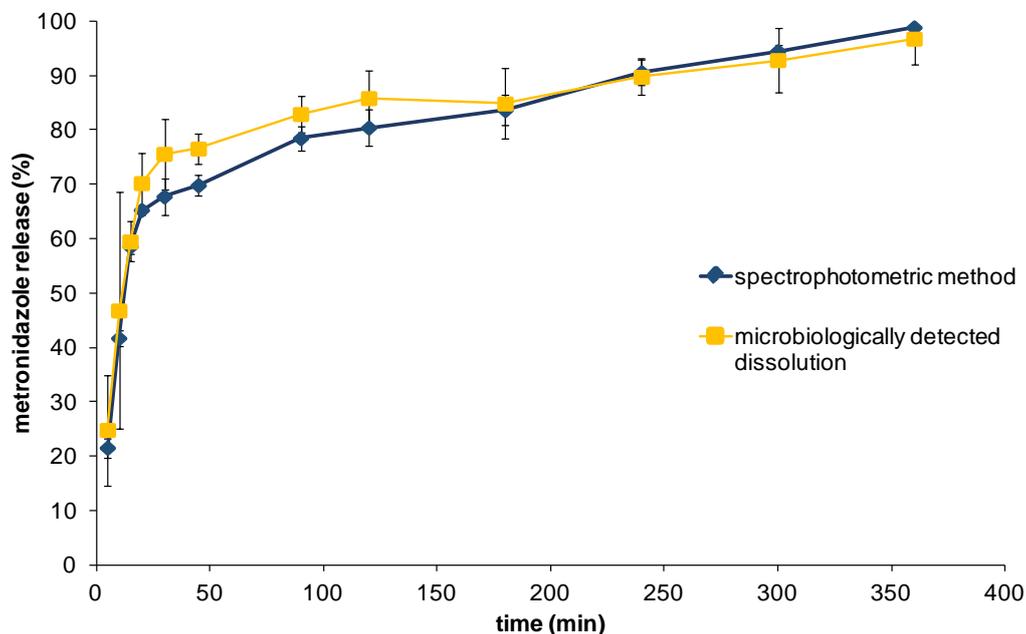


Fig. 6. Comparison of spectrophotometric and microbiologically detected dissolution of MF_OPT

In the *ex vivo* mucoadhesive studies, the two most frequently performed mucoadhesion measurements were done in order to present the potential in mucoadhesive properties of MF_OPT tablets: detachment force and rheological mucoadhesion studies.

Detachment force studies were carried with MF_OPT and three other tablets with modified composition as reference having sodium alginate, L-HPC B1 (MF_OPT_L-HPC) or both excipient (MF_OPT_EXC) absences from composition. The result of detachment force study is shown in **Fig. 7**. MF_OPT tablets have resulted in remarkably higher detachment force (505.49 ± 45.62 mN) compared to MF_OPT_L-HPC (314.91 ± 37.88 mN) and MF_OPT_EXC (264.68 ± 15.42 mN). Tablets without L-HPC B1 had higher detachment force, than the reference without both excipients. This study may show the potential in the possible physical synergistic effect between the applied gel forming polymer and disintegrant affected with rapid water absorption.

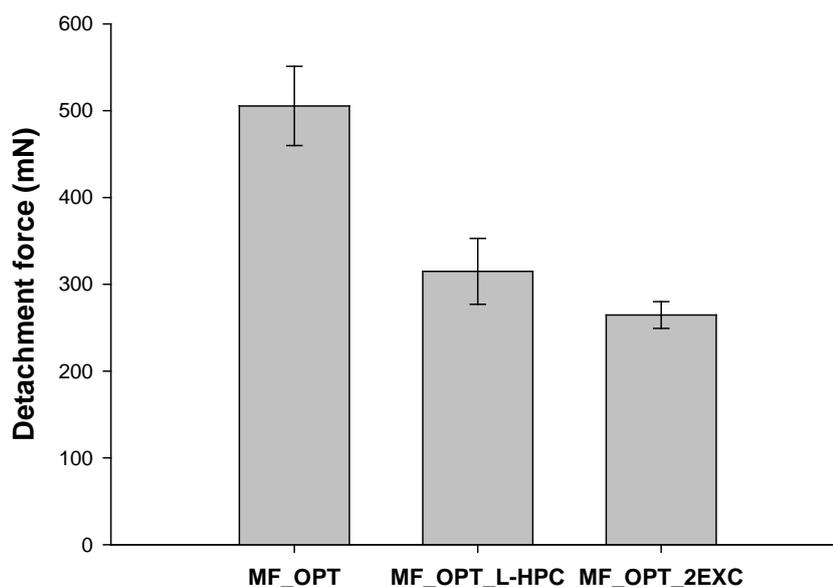


Fig. 7. Result of the detachment force study of MF_OPT (5.0 % sodium alginate, 38.63 % L-HPC B1, 8.45 % sodium bicarbonate)

Low viscosities were measured at 3 % mucus (7.63 ± 1.24 mPas) and at MF_OPT tablet dispersion (27.57 ± 23.22 mPas). Mixture of tablet and mucus showed significant rise of viscosity (846.89 ± 78.25 mPas at 2.63 1/s). Flow curve of mixture of tablet and mucus showed plastic flow behavior.

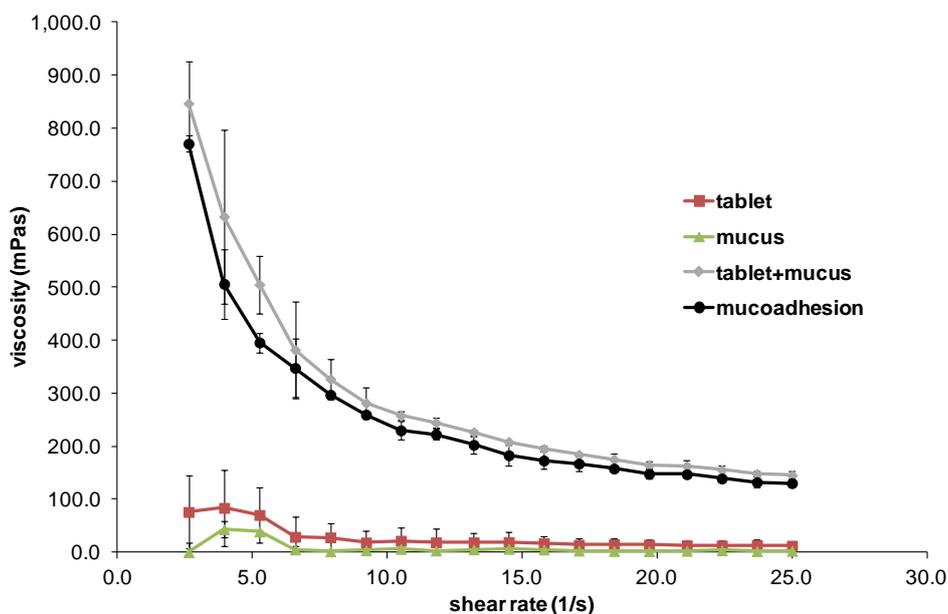


Fig. 8. Result of *ex vivo* rheological mucoadhesion studies of 3 % mucus, MF_OPT equilibrated to 3 % L-HPC and sodium alginate (tablet), their mixture (tablet+mucus) and calculated viscosity increase signed as ‘mucoadhesion’

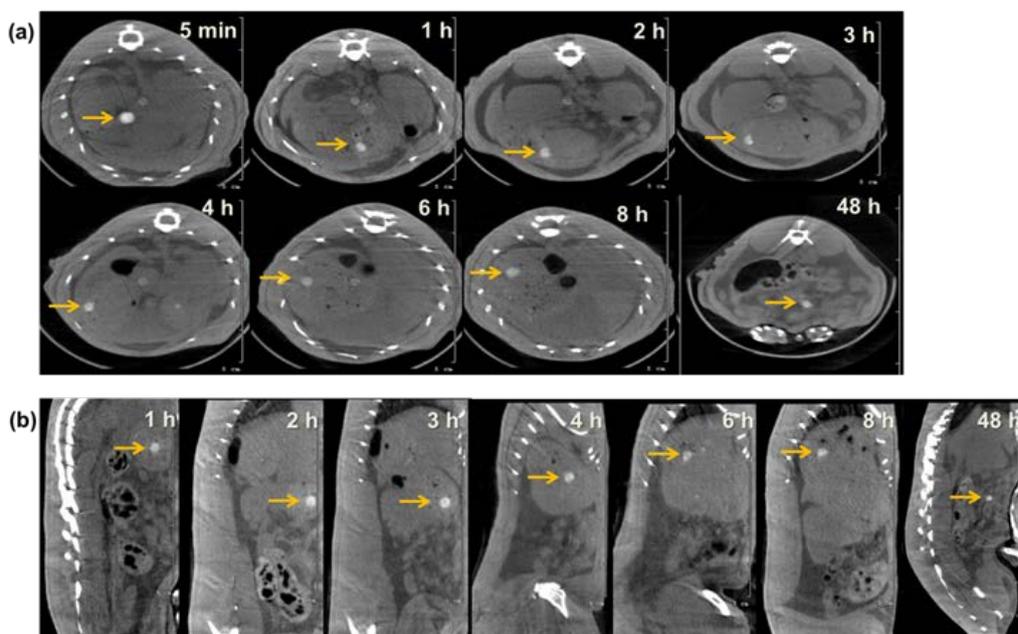


Fig. 9. X-Ray CT images of MF_OPT tablets loaded with 10 % barium sulfate at different time periods in transverse (a) and in sagittal plane (b) (location of tablets indicated with arrows)

Images (**Fig. 9**) showed the fact that MF_OPT tablets could remain in stomach for 8 hours.

This fine resolution X-Ray CT image (**Fig. 10**) visualized the voxels for the VOIs of tablet (indicated with yellow colors) and for VOIs of background (a conventional grey scale). With the application of this technique, valuable information could be gained related to the *in situ* behavior of tablets including disintegration, swelling, gas creation etc.



Fig. 10. Position of MF_OFT tablets in rat at 8 hours A: Identification of tablets with simple X-Ray CT evaluation; B: Identification and quantification of tablets with fine resolution X-Ray CT technique applying two different lookup tables

5. Summary of new results

Based on the evaluation of preliminary and optimization studies, new results of my research are the following:

1. Sodium alginate (high viscosity grade) was considered as a suitable matrix polymer in development of floating drug delivery tablets and its application resulted in rapid or sustained drug release depending on its concentration.
2. Differences between the types of L-HPC 11 and B1 were identified and were not remarkable at formulation studies. In the case of *in vitro* preformulation studies, more significant differences were observed at the evaluation of microscopic shape and size. In addition to L-HPC B1 showed better flowability, more intense wettability, thus this type was used in optimization project.
3. Summaries of statistically significant influences are shown in **Table 3** and **Table 4**. The mark of  indicates significance ($p < 0.05$),  is used when factor showed only trend ($p < 0.10$) and  presents absence of significance.
4. Remarkably high floating forces and fast start of buoyancy could be measured with the floating tablets in optimization project.
5. Optimization of factors could be done by the use of optimization criteria. The optimized composition contained:
 - 5.0 % sodium alginate (X_1),
 - 38.63 % L-HPC B1 (X_2),
 - 8.45 % sodium bicarbonate (X_3).
6. The optimized formulation showed promising properties including low floating lag time ($t_{lag} = 13.25 \pm 0.50$ s), high floating force ($F_{max} = 12.75 \pm 1.87$ mN) and biphasic drug dissolution.
7. Great similarity could be found in metronidazole dissolution detected by spectrophotometric and microbiological method ($f_1 = 5.231$; $f_2 = 66.613$).
8. Studies did not reveal any interactions between metronidazole and excipients.
9. Two frequently applied *ex vivo* mucoadhesion studies were performed, and optimized tablets have shown mucoadhesive properties. This result will promote our research team to examine *in vivo* mucoadhesion of this or similar floating tablets.

Table 3. Summary of significant influences in preliminary project

Preliminary project - significant influences	Applied model	Sodium alginate (% , X_1)	L-HPC (% , X_2)	L-HPC types (% , X_3)	Interaction ($X_1 X_2$)
floating lag time (t_{lag})	linear	✓	✗	✗	✗
total floating time ($t_{floating}$)	quadratic	✓	✓	✗	✓
maximal floating force (F_{max})	interaction (2FI)	✓	✓	✗	✓
time needed for maximal floating force (t_{Fmax})	quadratic	✓	✗	✗	✗
swelling capability (S_i)					
• from 30 min to 1 h	linear	✓	✗	✗	✗
• from 2 h to 4 h	linear	✓	✓	✗	✗
dissolution					
• from 5 to 45 min	quadratic	✓	✓	✗	✓
• from 45 min to 4 h	quadratic	✓	✗	✓	✗

Table 4. Summary of significant influences in optimization project

Optimization project - significant influences	Applied model	Sodium alginate (% , X_1)	L-HPC B1 (% , X_2)	NaHCO ₃ (% , X_3)	Interaction
floating lag time (t_{lag})	quadratic	✓	✓	✗	$X_2 X_3$
maximal floating force (F_{max})	linear	✓	✓	✓	✗
maximal floating force calculated for 100 mg ($F_{max/100mg}$)	linear	✓	✓	!	✗
time needed for maximal floating force (t_{Fmax})	-	-	-	-	-
dissolution					
• from 5 to 10 min	quadratic	✓	✗	!	✗
• from 30 min to 6 h	quadratic	✓	✓	✗	✗
SD values of dissolution data	linear	✓	✗	✗	✗

10. Detachment force *ex vivo* mucoadhesion results showed that L-HPC B1 could significantly improve the *ex vivo* mucoadhesion of sodium alginate. This phenomenon may open new possibilities to increase mucoadhesion properties of well know polymers without chemical modification.

11. X-Ray CT imaging result showed a prolonged *in vivo* retention of floating tablets in gastric region. Fine resolution images could be captured with the use of a special X-Ray CT technique. This technique with well-adjusted and defined parameters could allow not only tracking of the dosage form, but also possessing data about the *in situ* behavior of dosage form involving swelling, disintegration, and gas generation.

Publications and presentations related to the thesis

- I. **P. Diós**, S. Nagy, T. Pernecker, Sz. Pál, A. Dévay:
Influence of different types of low substituted hydroxypropyl cellulose on tableting, disintegration, and floating behaviour of floating drug delivery systems
Saudi Pharmaceutical Journal, 23 (2015) 658-666
IF: 1.283
- II. **P. Diós**, S. Nagy, Sz. Pál, T. Pernecker, B.Kocsis, F. Budán, I. Horváth, K. Szigeti, K. Böleskei, D. Máthé, A. Dévay:
Preformulation studies and optimization of sodium alginate based floating drug delivery system for eradication of *Helicobacter pylori*
European Journal of Pharmaceutics and Biopharmaceutics, 96 (2015) 196-206.
IF: 3.383
- III. **P. Diós**, A. Dévay:
Úszó tabletta előállításának biofarmáciai és gyógyszer technológiai optimalizálása (poster presentation)
Congressus Pharmaceuticus Hungaricus XV., Budapest, 2014
- IV. **P. Diós**, F. Budán, S. Nagy, I. Horváth, K. Szigeti, D. Máthé, A. Dévay:
Nátrium-alginát alapú efferveszcens úszótabletták *in vitro* és *in vivo* gyógyszer technológiai és biofarmáciai vizsgálata és optimalizálása (oral presentation, poster presentation, I. prize)
Cholnoky László Szakkollégium Nyitónap, Pécs, 2014
- V. F. Budán, **P. Diós**, L. I. Horváth, K. Andreidesz, I. Horváth, Z. Gyöngyi, Sz. Pál, B. Kocsis, K. Szigeti, D. Máthé:
Új távlatok – technológiai áttöréseken keresztül: úszó efferveszcens tabletták *in vivo* hatóanyag kioldódás vizsgálata Röntgen-CT-vel (poster presentation)
Cholnoky László Szakkollégium Nyitónap, Pécs, 2014
- VI. **P. Diós**:
Úszó hatóanyag-leadó rendszerek vizsgálata és optimalizálása (oral presentation)
Gyógyszerésztudományok Fóruma (Hungarian Society of Pharmaceutical Sciences, University of Pécs), Pécs, 2015
- VII. **P. Diós**, S. Nagy, V. Bognár, Sz. Pál, A. Dévay:
Hidrofil mátrixképző polimerek alkalmazhatósága efferveszcens úszó készítményekben (oral presentation)
I. Cholnoky László Szakkollégiumi Szimpózium, Pécs, 2015

- VIII. **P. Diós**, S. Nagy, T. Pernecker, Sz. Pál, A. Dévay:
Influence of sodium alginate and low-substituted hydroxylpropyl cellulose quantity in floating behavior and drug release in floating drug delivery systems (poster presentation)
6th BBBB Conference on Pharmaceutical Sciences, Helsinki, 2015
- IX. **P. Diós**, F. Budán, S. Nagy, I. Horváth, K. Szigeti, D. Máthé, Sz. Pál, A. Dévay:
Achievement of very high floating force and rapid dissolution of sodium alginate based floating drug delivery systems: *in vitro*, *in vivo* study (poster presentation)
6th BBBB Conference on Pharmaceutical Sciences, Helsinki, 2015
- X. **P. Diós**, F. Budán, K. Szigeti, I. Horváth, S. Nagy, T. Pernecker, A. Dévay, G. Gerencsér, Z. Gyöngyi, I. Kiss, Sz. Pál, D. Máthé:
Parameters of floating drug delivery systems - tracked in animal model utilizing *in vivo* X-ray CT imaging (poster presentation)
6th BBBB Conference on Pharmaceutical Sciences, Helsinki, 2015
- XI. D. Máthé, F. Budán, Sz. Pál, I. Kiss, **P. Diós**, K. Szigeti:
X-Ray CT Imaging of Stomach Passage of Contrast-Enhanced Floating Tablets in a New Rat Model (poster presentation)
European Association of Nuclear Medicine Congress, Hamburg, 2015

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- CROmed Translational Research Centers, Budapest,
- Department of Biophysics and Radiation Biology, Semmelweis University
- Department of Pharmacology and Pharmacotherapy, University of Pécs,
- Department of Public Health Medicine, University of Pécs,
- Department of General and Physical Chemistry, University of Pécs.