

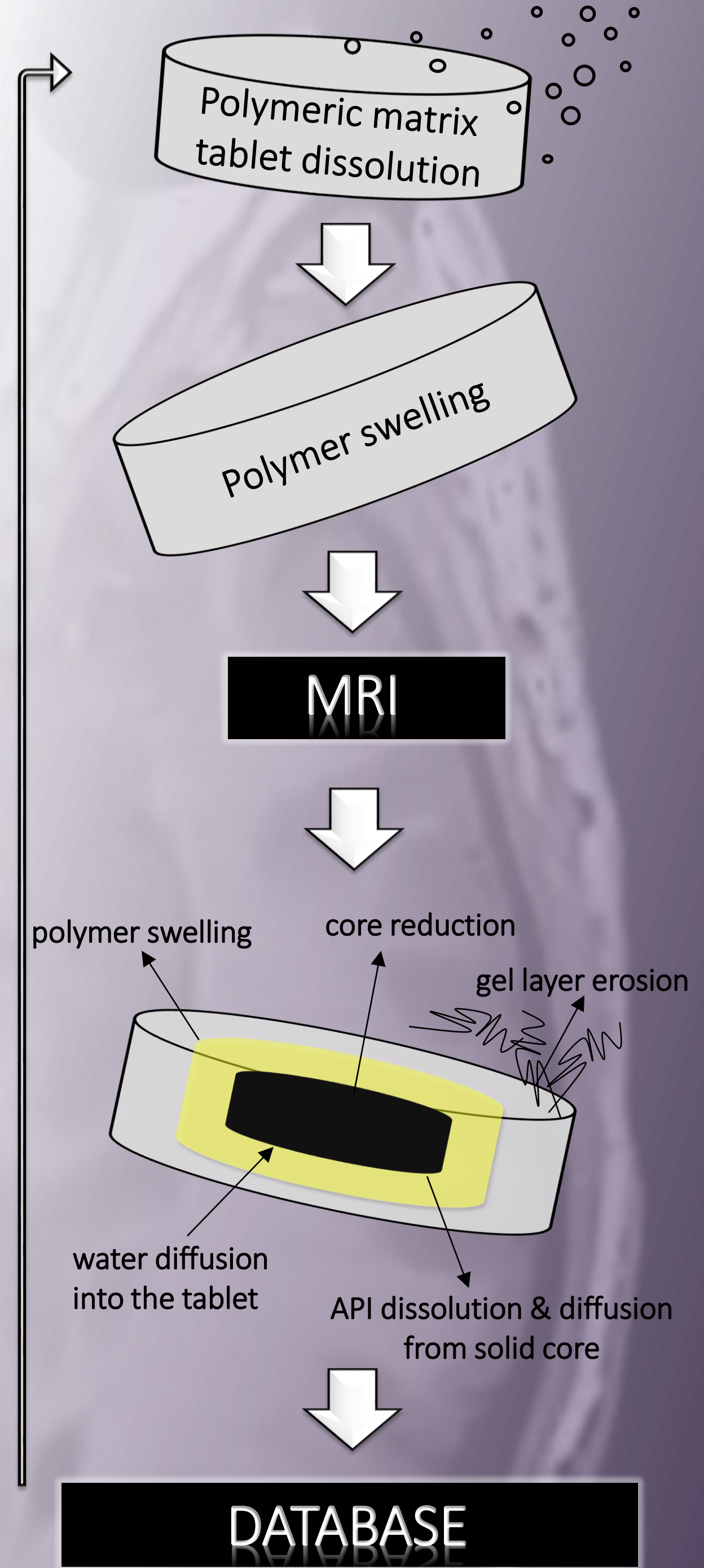
Measurement of the polymer swelling kinetics, comparison of two different techniques - MRI imaging and Texture analyzer

M. Gajdošová^{1,*}, N. Sarvašová¹, D. Pěček², F. Štěpánek¹

¹Department of Chemical Engineering, Institute of Chemical Technology, Prague, ²Zentiva, k.s., U Kabelovny 130, Prague 10, Czech Republic; *E-mail: Michaela.Gajdosova@vscht.cz

Introduction

- Sustained-release formulations offer the solution for many problems of oral drug delivery systems
- hydrophilic and hydrophobic polymers



- polymeric matrices
- additives
- technological parameters
- the effect on API release kinetics

Motivation:

- to design the experiments in a flow-through cell for MRI measurements
- to monitor the swelling of different types of matrices in time
- to compare the results obtained by MRI and Texture analyzer

Materials & Methods

Chemicals: hypromellose - HPMC (Methocel K4M a K100M), polyethylenoxid - PEO (Polyox WSR 303 NF) and hypolose - HPC (Klucel HXF), carnauba wax (Mach Chemicals s.r.o.). Magnesium stearate (Peter Greven, Bad Münstereifel) and anhydrous colloidal silicon oxide (Aerosil 200, Degussa) as excipients were used. As a model API, highly water soluble levetiracetam (Zentiva k.s.). For dissolution experiments phosphate buffer saline (PBS; pH=6) was used. As a contrast agent in MRI experiments magnetic composite FeO_x SiO₂ nanoparticles were used (FeO_x nanoparticles stabilized with sodium citrate, ethanol (purity - UV/VIS), 24% ammonia solution, Tetraethyl orthosilicate (Sigma Aldrich))

Tablet preparation

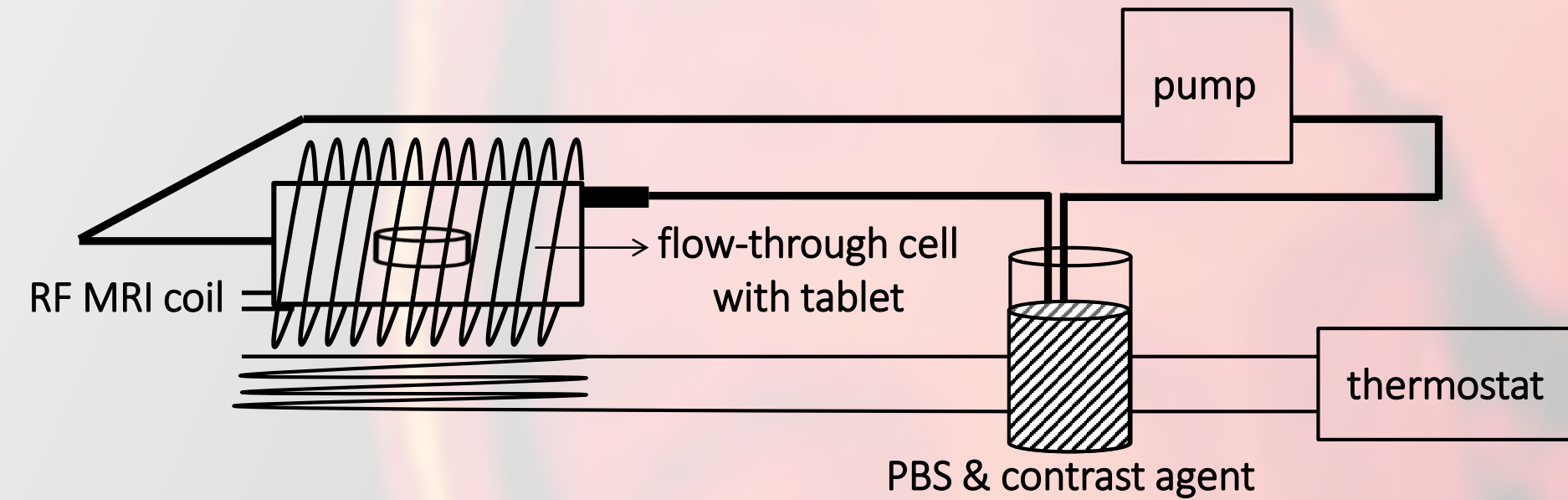
- direct compressing of previously homogenized mixture of API and excipients (10 min)
- lenticular, diameter 10 mm

D. Pěček, M. Štýbnarová, E. Mašková, P. Doležel, M. Kejdušová, D. Vetchý, K. Dvořáčková, Využití analýzy textury při vývoji a hodnocení matricových tablet s prodlouženým uvolňováním léčiva, Chem. Listy, 108 (2014) 483 - 487

The amount of substances in tablet (mg/tbl)*						
Tablet	Levetiracetam	CW	HPMCK 100M	HPMC K4M	PEO	HPC
1	100	-	230	-	-	-
2	100	-	57.5	172.5	-	-
3	100	-	-	-	230	-
4	100	-	-	-	-	230
5	100	115	115	-	-	-
6	100	115	-	-	115	-

*each sample contained 2.5% of magnesium stearate and 0.5% of Aerosil

Dissolution experiments in MRI



Tablet	Echo time [ms]	Matrix size	BW[Hz]
1	16	128x128	3200
2	18	128x128	2000
3	20	96x96	2000
4	16	128x128	3200
5	18	128x128	2000
6	18	128x128	2000



- MSME protocol
- repetition time: 2000 ms
- number of averages: 2
- field of view: (1.8x1.8) cm
- 3 axial slices
- slice thickness: 1mm
- medium – PBS (pH = 6)
- temperature - 37±2°C
- flow rate - 4 ml/min
- 4 - 8 h

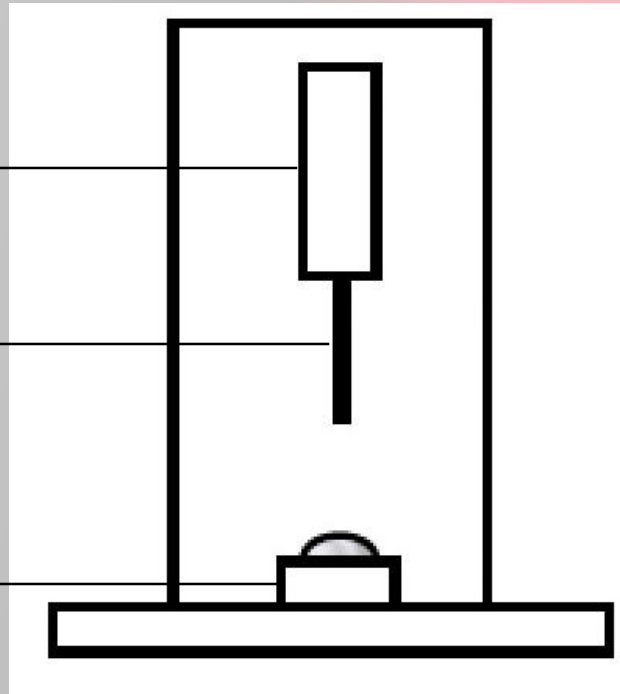
Dissolution experiments and the analysis of texture

- 4 tablets under the same conditions (paddle dissolution test in USP 2 cell)
- measurements in times 0.5; 1; 2; 4 and 8 hours

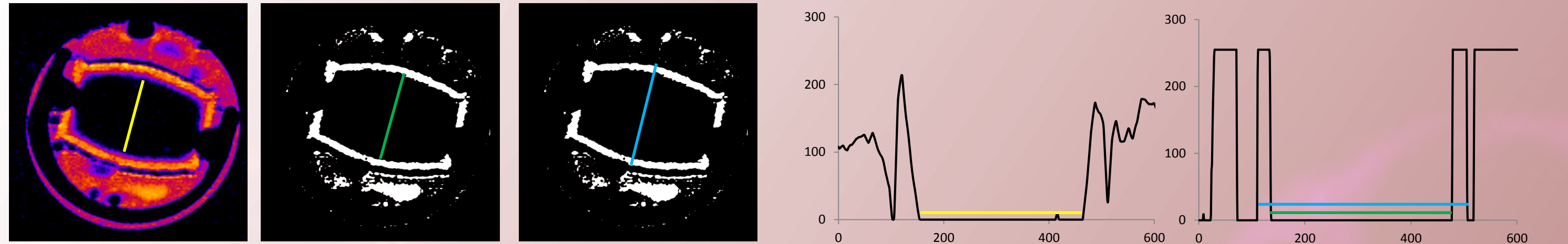
vertically sliding arm

cylindric probe with a flat tip TA39

matrix tablet in holder



Results & Discussion

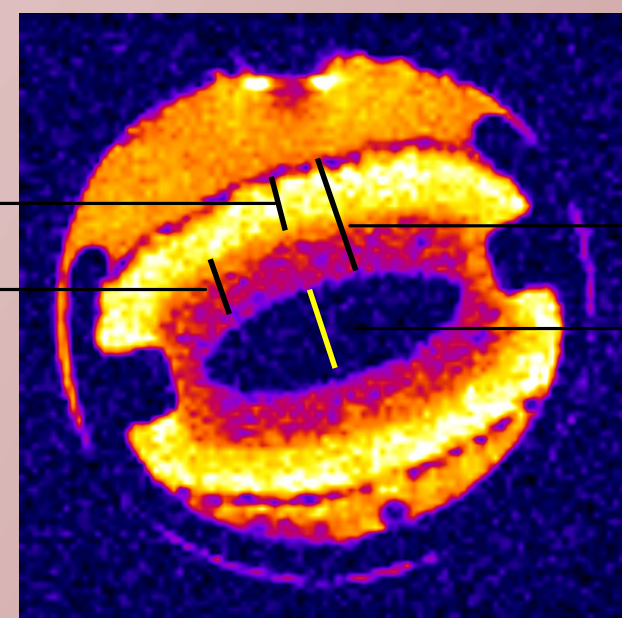


- ImageJ
- Adjusted brightness and contrast
- plot profile across the whole tablet
- Distances between layers in pixels, then converted to mm

Another possibilities of polymer swelling kinetics evaluation:

highly swollen gel layer

moderately swollen gel layer



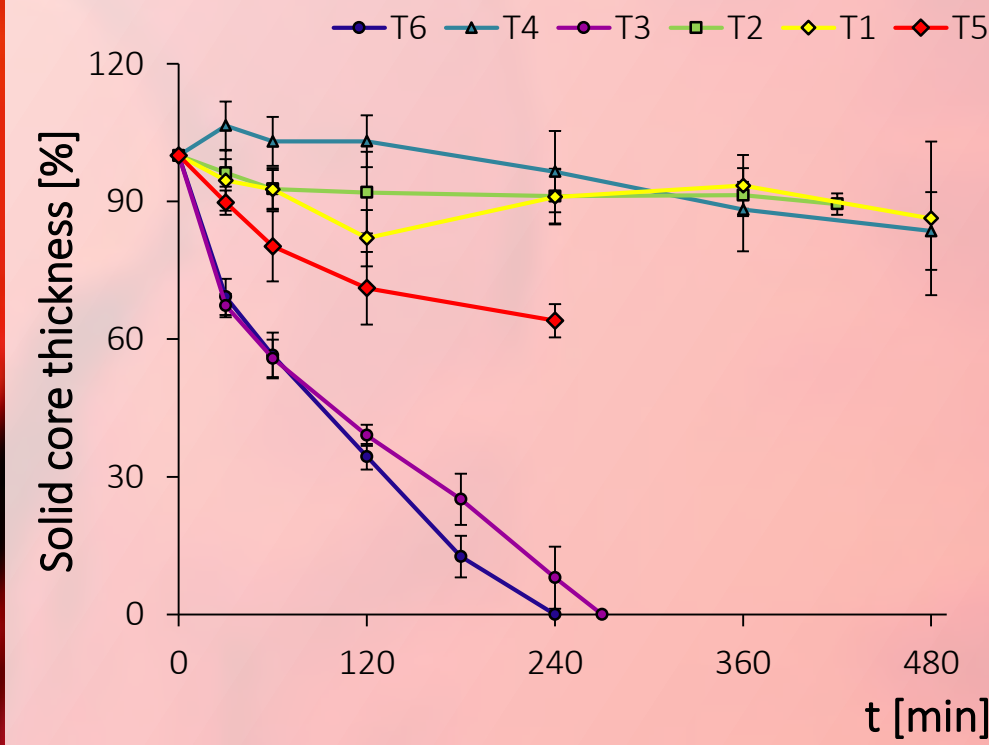
gel layer

solid core

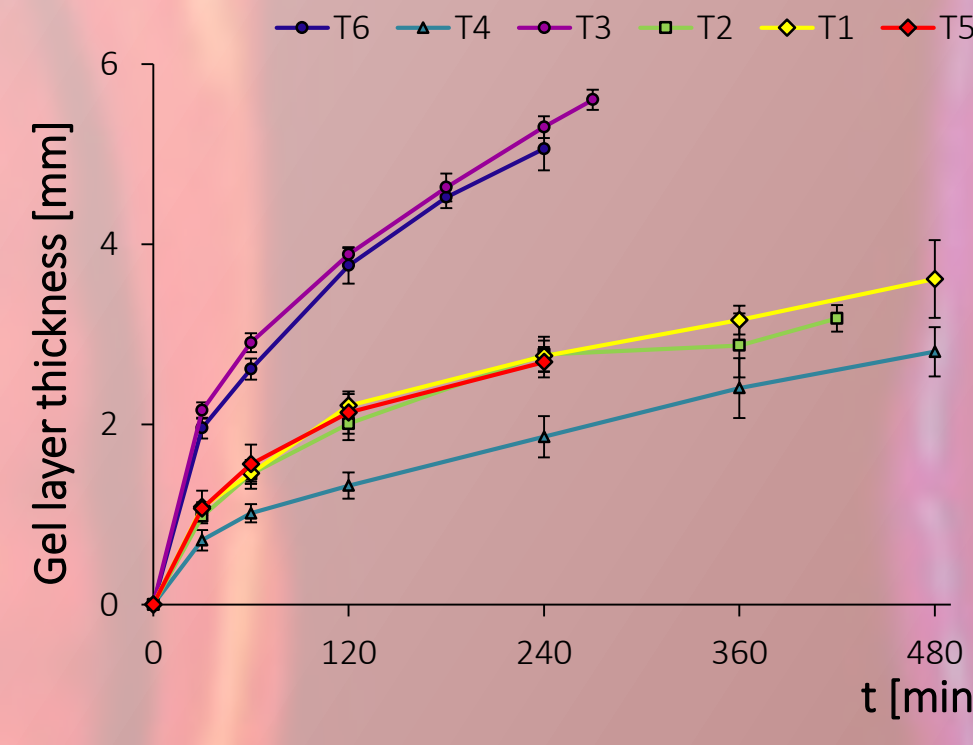
MRI results

- Each tablet was measured three times and the gel layer was evaluated in three different regions

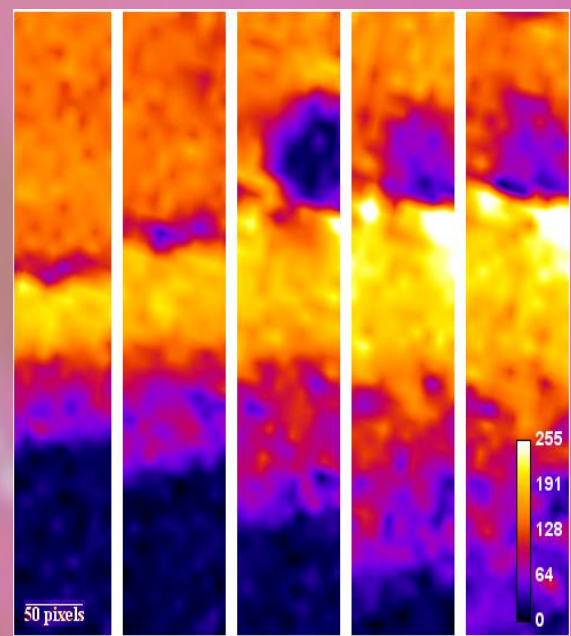
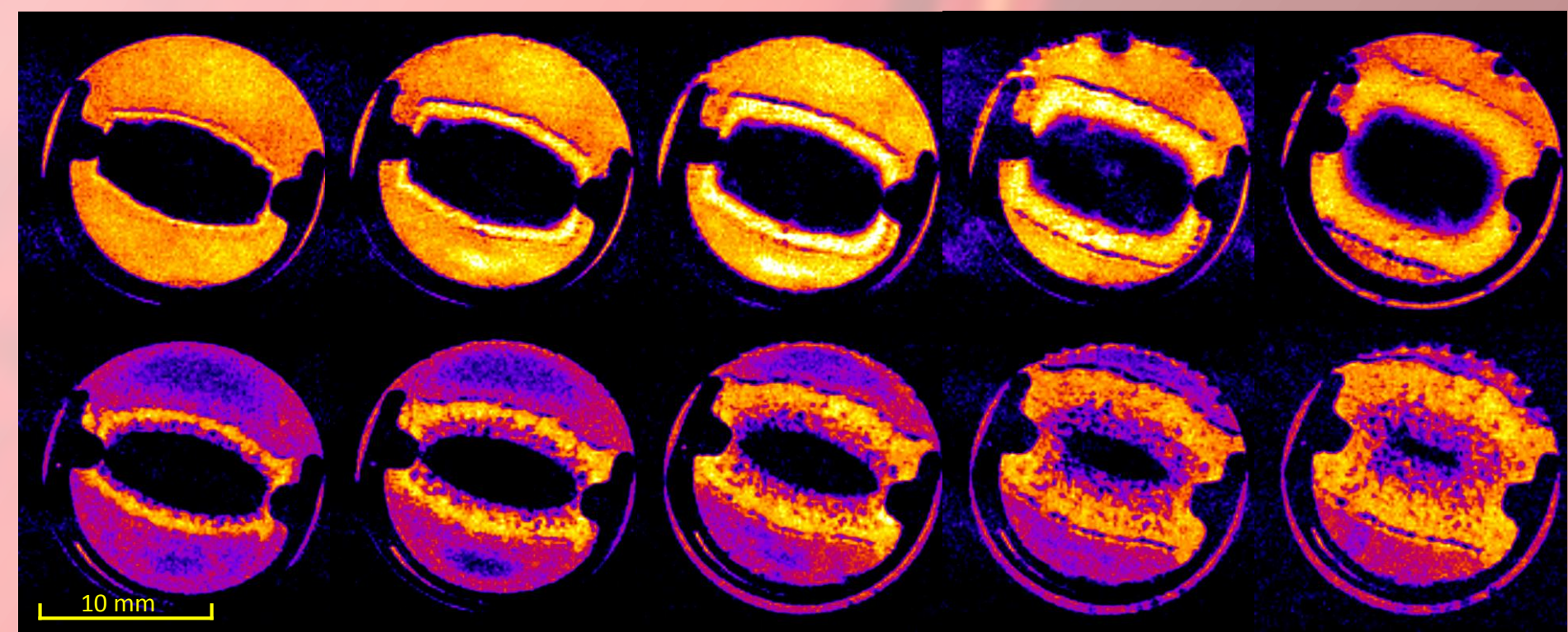
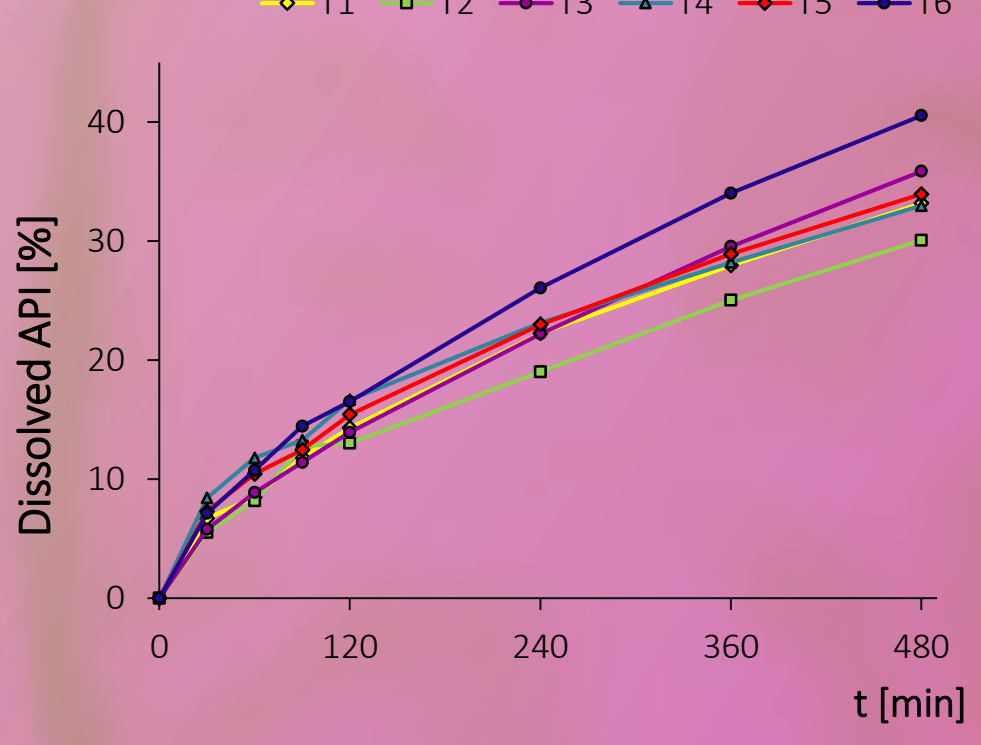
Solid core thickness



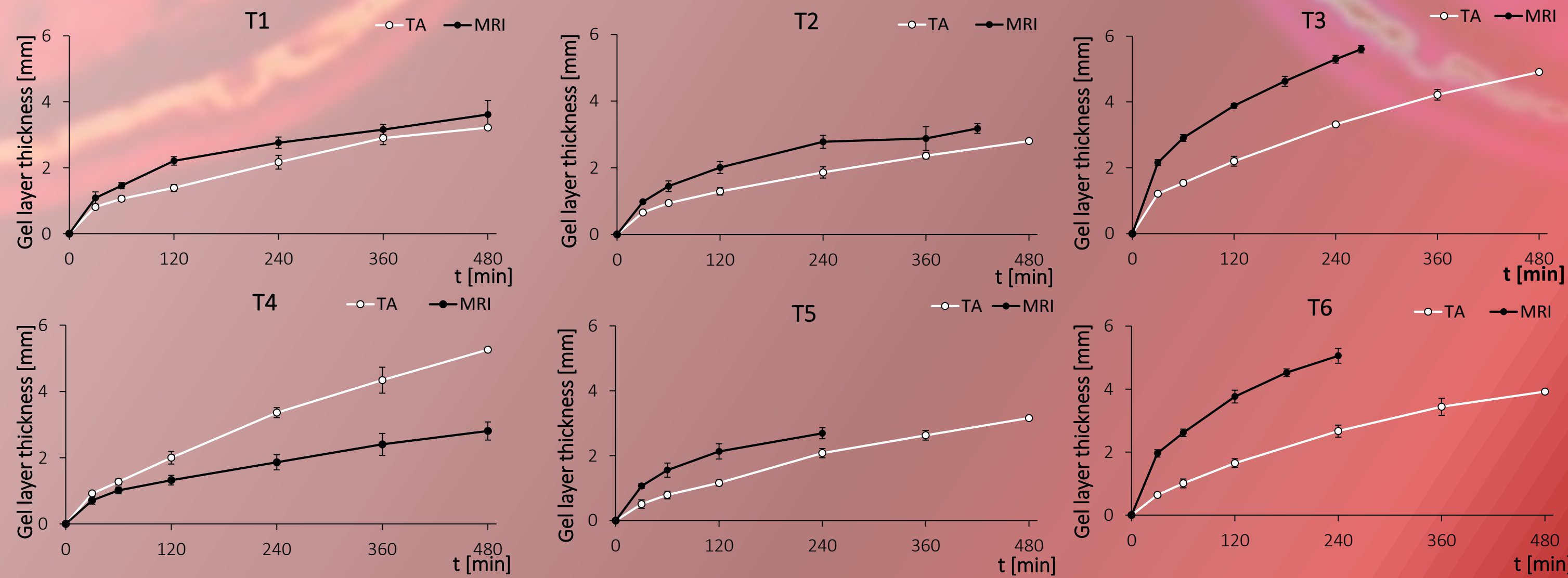
Gel layer thickness



API dissolution



Comparison of MRI and texture analyzer obtained results



Conclusions

MRI turned out to be a suitable imaging method for polymer swelling quantification. With the complementary methods, such as texture analysis, X-ray μ CT or ATR-FTIR, it can lead to the proper understanding of processes occurring during the polymeric matrix dissolution. The results may not be fully explained yet, but this study is only a first small step in a bigger project. For the future measurements, the effect of different additives on the polymer swelling kinetics will be evaluated. The results from the whole research should lead to the database of matrix components and conditions of technological processes and their effects on the dissolution profile of API, thus simplifying the formulation of dosage forms with the desired drug release.