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Summary of the Ph.D. thesis

STUDY OF THE WIDELY USED ETHYLCELLULOSE POLYMER AS FILM FORMING AND MATRIX FORMER AGENT

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1. INTRODUCTION

With the continuous development of biopharmacy and technology, the possibility arose to make controlled-release release oral systems and with this the potential to control the rate, place or duration of drug release. Accordingly, modified (sustained, retarded, pulsatile) drug release can be achieved; and the one possible way to realize this is to use a properly formed coat (pH-dependent dissolution, diffusion film, etc.). These solutions require film coats to meet higher expectations.

There are several methods to achieve modified drug release (MR). One of the most common way to prepare this dosage form, is film coating. Another method is, to formulate a multiparticulate drug delivery system.

Multiparticulates involve multiple-unit small systems. They have more advantages compared to single unit systems owing to their small size. They are better distributed in the gastrointestinal transit, therefore cause less side effect.

2. AIMS

The two main parts of this work were to investigate the widely used ethylcellulose (EC) polymer as a film forming agent and as a matrix former agent.

In the first section, two ethylcellulose *film forming* polymers with different chain lengths and different molecular weight (Ethocel Standard Premium 10®, Ethocel Standard Premium 45®, Colorcon Ltd.) were studied. The investigation of free films is an essential part of the preformulation studies because it is necessary to know weather the given formulation is suitable to coat the corpus or not.

The aim of our research was to investigate the effect of the length of the polymer chain and the effect of the concentration of triethyl citrate (TEC), which was used as a plasticizer, on the thermal stability of the film and as well as on the structure of the ethylcellulose films (EC10 and EC45) used for preparing MR dosage forms. The influence of storage time was studied by monitoring the changes in the thermoanalytical parameters and by performing Termogravimetric Analysis coupled with Mass Spectrometry (TG-MS) examinations. The structure analysis and the incorporation of the plasticizer were performed with the use of Fourier transform infrared spectroscopy (FT-IR). There are several methods for the prediction of the polymer-plasticizer interactions [5], but the real microstructure and the incorporated amount of the plasticizer could be studied with the use of FT-IR spectroscopy [6-11]. The distribution of the plasticizer between the chains of the polymer ethylcellulose was

determined in order to explain the mechanical properties. The distribution was investigated with Positron Annihilation Lifetime Spectroscopy (PALS), and the mechanical properties with breaking hardness tests. The best film-former with plasticizer was chosen with the optimal concentration. Selection of the optimum type and concentration of the plasticizer is essential in the formulation of pellets and coated dosage forms.

In the second section, ethylcellulose polymer was used as matrix former excipient. Besides the generally used microcrystalline cellulose (MCC), EC was used as matrix former to achieve modified drug release ensured by diffusion. Innovative, matrix pellets containing capsule dosage forms was developed with combined Active Pharmaceutical Ingredients (API).

The matrix pellets were made by extrusion-spheronization using a twin-screw extruder. Two different APIs with different Biopharmaceutics Classification System (BCS), solubility and particle were used in the course of formulation of monolithical matrix pellets. Some pellet properties (aspect ratio (AR), 10% interval fraction, hardness, deformation process) were determined. The aim of our study was to investigate how the two different APIs with different solubility and particle size influence the process.

3. SECTION I.

3.1. Materials

Ethocel Standard Premium 10® (EC10), and Ethocel Standard Premium 45® (EC45) (Colorcon Ltd., Dartford, England) were used for the experiments, which differ in the viscosity of their solutions and in the length of the polymer chains. As polymers do not dissolve in water, only in organic solvents; we used 96 % alcohol as solvent. Plasticizers have the ability to alter the physical properties of a polymer film. During our experiments we used triethyl citrate (Ph. Eur.) (TEC) as plasticizer, which is the ethyl ester of citric acid, it belongs in the group of organic esters.

3.2. Preparation of free films

For the experiments alcoholic solutions with 10% polymer content were prepared without plasticizer and with 1-3-5% triethyl citrate concentration. The solutions were sprayed on teflon surfaces placed in a rotating vessel. Before the preparation of free films, the Minimum Film forming Temperature (MFT) of EC films of various compositions were determined (Table 1.), so that the temperature of the drying air during spraying could be set accordingly.

The properties of the prepared free films were determined after preparation (fresh) and also after 1, 2 and 4 weeks of storage (40°C/50RH%) in order to monitor changes.

Table 1: MFT values of EC10 and EC45 films

		CONCENTRATION OF PLASTICIZERS			
		0%	1%	3%	5%
EC10 films	*MFT* (°C)	26.1	20.7	20.3	17.7
EC45 films	*MFT* (°C)	24.4	13.1	16.8	18.8

After the evaluation of the data shown in the Table 1., it was found that the use of plasticizer decreased the value of MFT in each case. The increase of triethyl citrate concentration decreased the MFT value proportionally to concentration in the case of EC10 films and according to the minimum curve in the case of EC45 films.

3.3. Results and discussion

3.3.1. Thermoanalysis

The condition of the formation of a proper film structure is to know the glass transition temperature of the film forming polymer, which was determined with a DSC instrument. Both the structure and the glass transition temperature of the film are influenced greatly by the properties and concentration of the plasticizers used, therefore their role was studied. The numerical data of glass transition are summarized in Table 2.

Table 2: Changes in the T_g values of EC10 and EC45 fresh films as a function of plasticizer concentration

		Triethyl citrate concentration			
		0%	1%	3%	5%
EC10	Glass transition temperature (Tg)/°C SD	126.4 (±2.22)	126.9 (±2.74)	118.6 (±7.89)	105.1 (±8.95)
EC45	Glass transition temperature (Tg)/°C SD	133.4 (± 0.56)	135.9 (± 0.23)	141.5 (± 0.43)	128.7 (± 0.91)

The DSC curves of EC10 fresh films containing various quantities of TEC are shown in Figure 1a, the curves of EC45 fresh films in Figure 1b. In the case of EC10 films, the glass transitions are indicated on the curve and it is clear that the T_g value decreases with the increase of the plasticizer concentration. It is clear from the data that the T_g value in fresh

films is increased by 3% plasticizer, but is decreased by 5% of plasticizer in the case of EC45 films, which is again due to structural changes (Fig. 1b).

The comparison of the glass transition temperature values of the two film forming polymers shows that the glass transition temperature of films prepared from the shorter-chain EC10 polymer is slightly lower than for longer-chain EC45 films.

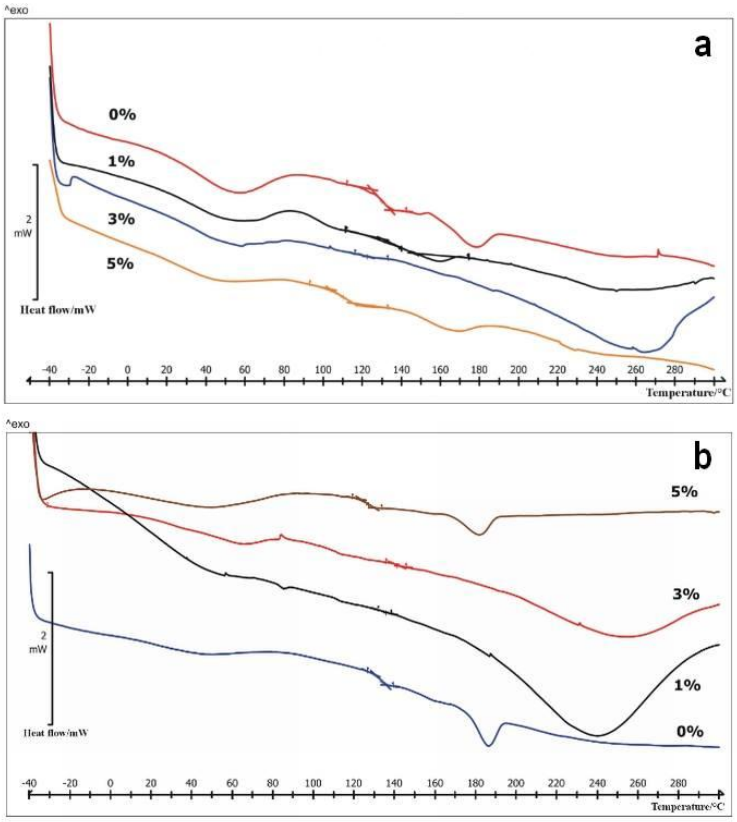

Figure 1.: DSC curves of EC10 (a) and EC45 (b) fresh films

It was found that the glass transition temperature of films prepared from the shorter-chain EC10 polymer with a "looser" structure is slightly lower than for longer-chain, more "compact" EC45 films. In fresh films containing plasticizer the T_g value could be decreased by 3% plasticizer in the case of "looser" EC10 films prepared from shorter-chain polymers, while 5% plasticizer was needed for "stronger" EC45 films made from longer-chain polymers (Fig.1b.). EC45 films were more stable during storage. The thermal stabilities of the two polymers are approximately the same. The thermal behaviour of TEC and of films containing 5% plasticizer is shown in Figure 2. The TG curves show that the decomposition of TEC starts as early as over 120 °C and becomes more intensive over 200 °C, and the material is fully decomposed before reaching 300 °C. The shape of the curves is a proof for TEC

probably being built in the structure of the EC film, because its decomposition from the film starts only later, at about 180-200 °C.

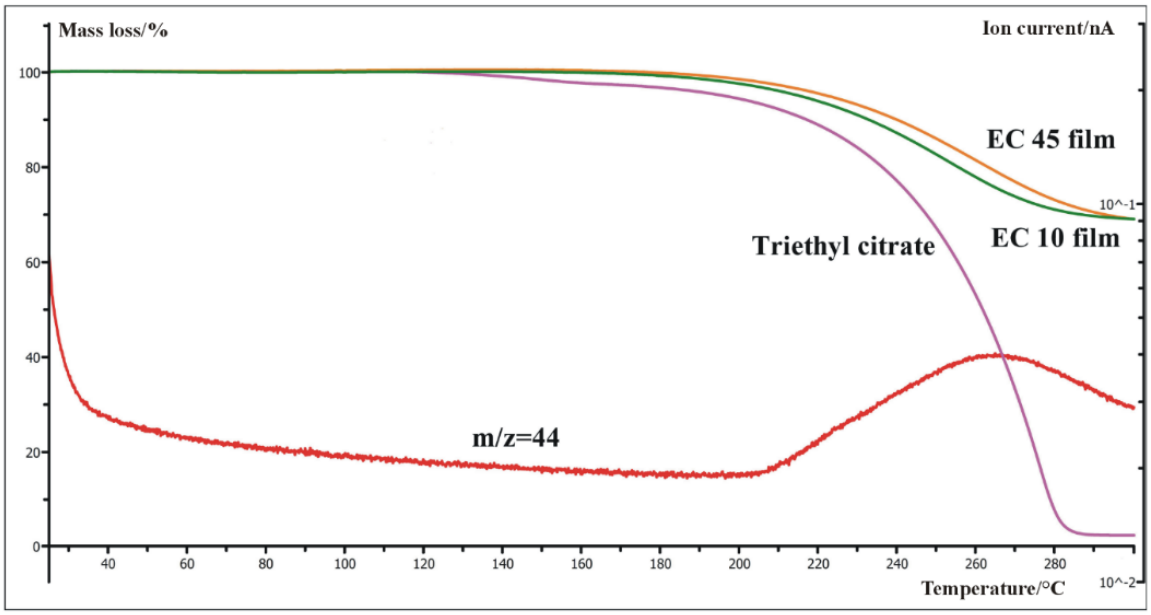

Figure 2.: TG curves of EC10 and EC45 films containing 5% triethyl-citrate and their MS evaluations

3.3.2. Physico-chemical properties of films

The incorporation of TEC into the structure will affect not only the mechanical and thermal properties but also the surface characteristics of films. The structure of films and the incorporation of plasticizer can be followed with the use of FT-IR (Fig.3.).

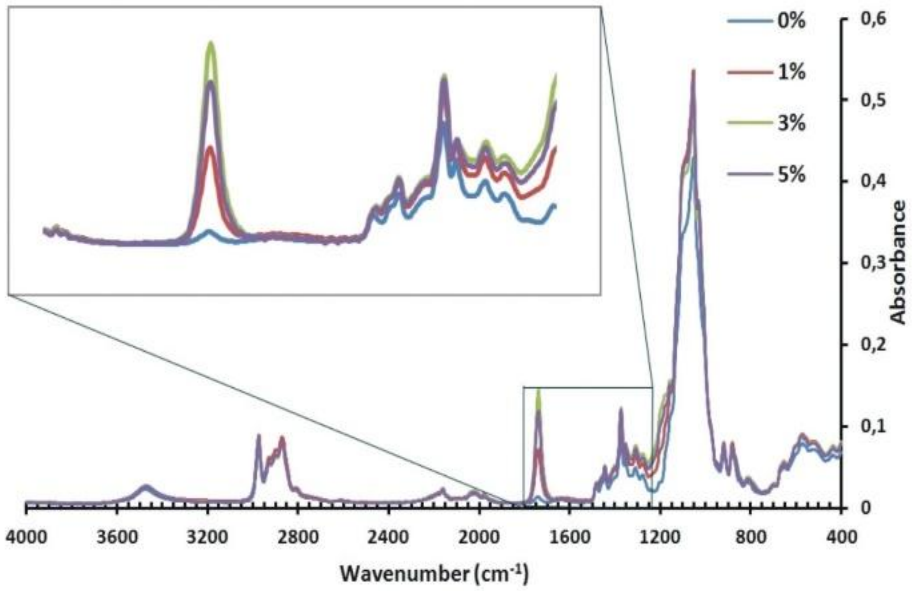

Figure 3.: FT-IR spectra of the EC45 films

However, longer chains resulted in higher lipophilicity, probably due to the relatively increased proportion of the ethyl ether groups. The incorporation of triethyl citrate into the structure will affect not only the mechanical and thermal properties but also the surface characteristics of films The results support that only a limited amount of plasticizer can be incorporated with physico-chemical bindings into the structure of polymer films and this proportion will basically determine some of the main properties of the preparations.

PALS studies demonstrated that up to a concentration of ~1 % the incorporated plasticizer is integrated between the polymer chains (Fig.4.). The positron lifetime initially decreased slightly at the lowest plasticizer concentration. This is a consequence of the distribution of the plasticizer molecules between the polymer chains, filling the free-volume holes, occupying sites formerly available for the positronium atoms, providing a higher electron density. The lifetime of the positronium atoms therefore decreases. The structure of the film was changed as a result of the admixture of the plasticizer. At higher concentrations, the plasticizer initiated a large-scale rearrangement of the polymer chains, leading to the formation of larger free-volume holes, as indicated by the longer lifetimes. It should be emphasized that the PALS data did not indicate any major structural change up to a plasticizer concentration of 1%. The large-scale rearrangement of the polymer chains necessitated a higher concentration.

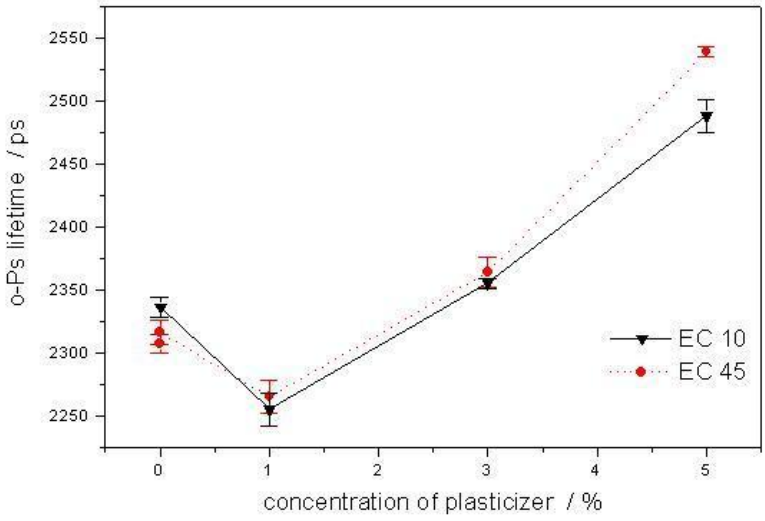

Figure 4.: Positron lifetime plotted against concentration

The mechanical properties were clearly revealed to depend on the concentration of the plasticizer.

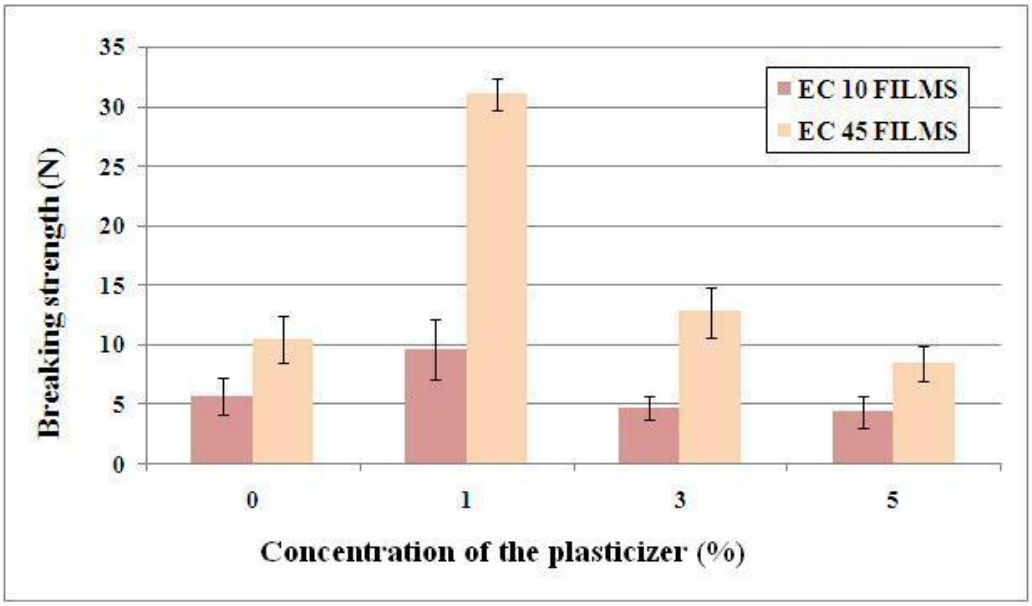

Figure 5.: Breaking strength of EC10 and EC45 free films

The breaking strengths of the two kinds of ethylcellulose films are compared in Figure 5. It can be seen that the breaking strengths of the films prepared from the shorter-chain Ethocel 10 polymer with its looser structure were lower than those for the longer-chain, more compact Ethocel 45 films. Ethocel 45 formed a significantly stronger structure.

The ideal concentration of the plasticizer in these film-formers was 1%. This concentration resulted in strong, mechanically resistant, stable films. This composition can be used for diffusion coating to obtain a product with modified release.

4. SECTION II.

4.1. Materials

Ethocel Standard 10 FP Premium (Colorcon Ltd. Dartford. England) was used as matrix former and MCC type 101 (Avicel 101, FMC Corporation, Philadelphia, USA) as pharmaceutical excipient (filler and binder). A mixture from 1% triethyl citrate (TEC), in an aqueous ethanol solution 96% (V/V) and deionised water were used as granulation liquid. Two APIs with different properties were used. Enalapril maleate (BCS III.) and hydrochlorothiazide (BCS IV.) combination is used to treat high blood pressure. Hydrochlorothiazide reduces the hyperkalaemia caused by enalapril maleate.

4.2. Factorial design

The study dealt with the effect of 3 process parameters - spheronization time (x_1), the liquid feed rate (x_2), and the speed of the friction plate (x_3) – on the pellet properties (shape, tensile strength, breaking force). Mixed 2 and 3 level factorial design was applied to optimize the process parameters and the best composition for the experiments. We examined the liquid feed rate (x_2) and the speed of the friction plate (x_3) on 3 levels, while the effect of spheronization time on 2 levels. These dependent variables influenced the properties of the pellets. Statistica for Windows 11 AGA (Statsoft. Inc. Tulsa. USA) software was applied to determine the effects of the factors. The effect of the factors was evaluated with the use of Statistica for Windows 11 (AGA software). The experimental plan can be seen in Table 3.

Table 3.: Experimental plan

FACTORS	LOW (-)	ZERO (0)	HIGH (+)
x_1	2.5 min	-	10 min
x_2 (EM) **x_2 (HCT)**	25 g/min 26.3 g/min	27 g/min 28.5 g/min	29 g/min 30.7 g/min
x_3	1000 rpm	1250 rpm	1500 rpm

4.3. Preparation of pellets

1500 grams of powder mixture was prepared from 20% of API (enalapril maleate or hydrochlorothiazide), 30% of ethylcellulose and 50% of microcrystalline cellulose.

The powders were combined in a laboratory-scale blender (LM40, Bohle, Ennigerloh, Germany) and then transferred into the gravimetric powder feeder (B: KT 20, K-Tron Soder, Lenzhard, Switzerland) of the extruder. The co-rotating twin-screw extruder (Mikro 27GL-

28D, Leistritz, Nuremberg, Germany) was equipped with an axial screen with 23 dies of 1 mm diameter and 5 mm length. The extrusion took place at a constant screw speed of 100 rpm, a powder feed rate of 33 g/min and a liquid feed rate according to the experimental plan. Deionised water, 96% ethanol and 1% TEC were used as granulation liquid supplied by a membrane pump (C. Cerex EP-31, Bran and Luebbe, Norderstedt, Germany) Batches of 40 g resultant strands of extrudates were collected and spheronized in a spheronizer (Caleva 120, Sturminster Newton, UK) according to the design of experiments. The particles were dried in a fluid bed apparatus (GPCG 1.1., Glatt, Dresden, Germany) for 20 min with an inlet air temperature of 60°C.

4.4. Results and discussion

4.4.1. Characterization of API

Both APIs have tabular crystal habit (Fig. 6.), and heterodisperse size distribution (Table 4.). The most considerable difference between the APIs is particle size. EM crystals are tenfold bigger than HCT particles.

A further difference is that whilst EM crystals are well-developed and sometimes covered by tiny, irregularly-shaped crystal grains (Fig. 6a), the edges and corners of the HCT crystals are rounded (Fig. 6d, e, f). The sticking of smaller particles on the surface of larger crystals, - which suggests a strong cohesion between them is also characteristic for HCT. That is why a number of irregular looking crystals are visible at small magnifications (Fig. 6b), with the presence of some big crystal agglomerates. It is well visible at higher magnifications (Fig. 6d, e, f), that the smaller particles are irregular aggregates of few tabular crystals, while bigger agglomerates are formed from undeveloped particles (Fig. 6c) and behave as individual units in the product.

As it can be seen, except for the solubility and particle size, the general physical properties of the APIs are similar, and their mechanical behaviour during the extrusion-spheronization process is expected to be similar too.

Table 4.: Properties of API's

	Enalapril maleate	**Hydrochlorothiazide**
Aspect ratio	1.866	1.829
Roundness	0.595	0.63
Mean Feret diameter (µm)	67.4 (±43.84)	5.57 (±3.96)
Aqueous solubility (mg/ml)	25	0.722

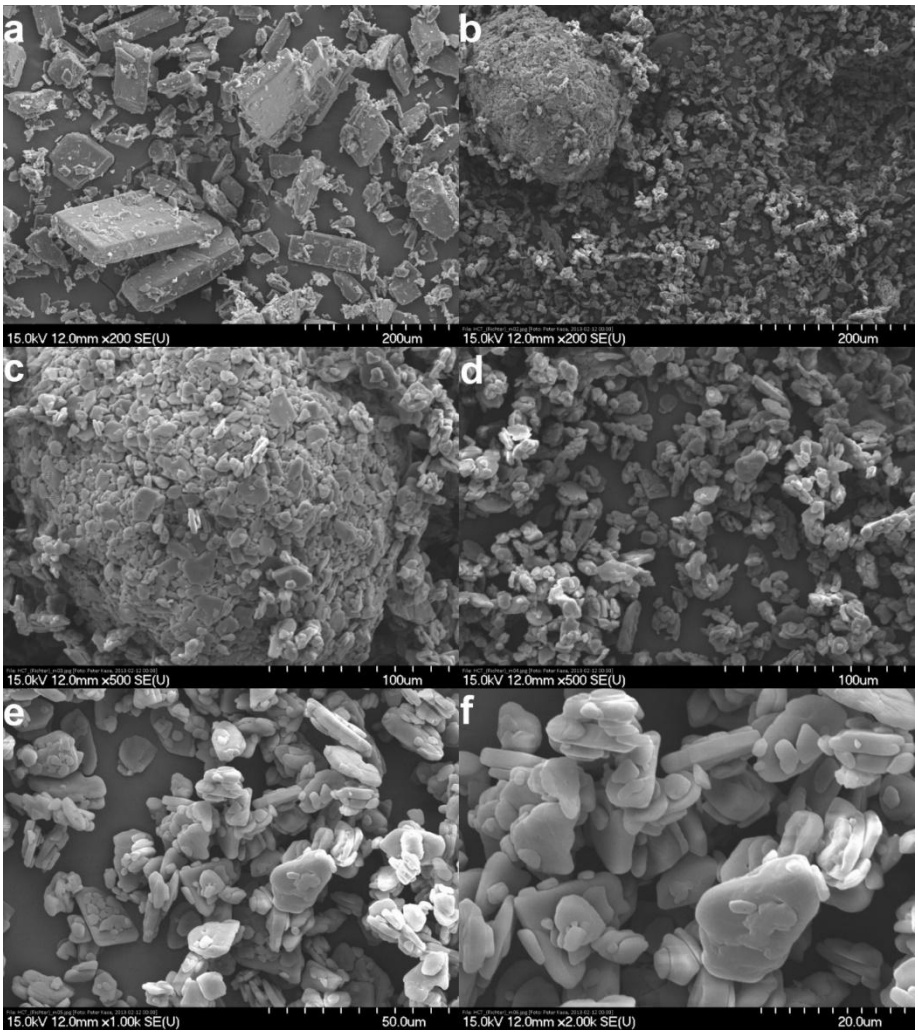

Figure 6.: SEM picture of EM (a), and HCT in magnification 200x (b) 500x (aggregate) (c), 500 x (individual crystals) (d), 1000x (e) and 2000x (f)

4.4.2. Characterization of pellets

We can define pellets as spherical, free flowing granules with a narrow size distribution, that typically varies between 0.50 and 1.50 mm. All experimental settings resulted in pellets for both formulations with a mean average Feret diameter from 1.0 to 1.5 mm. The shorter spheronization time results in larger size particles. The reason for this phenomenon is that the particles do not have enough time to get a rounded shape, and thus “bone” shaped particles are formed during spheronization, the particle size of which is larger as well.

The 10% interval is used to characterise the particle size distribution., which describes the fraction of pellets within the interval 0.9-1.1 of the dimensionless diameter. The fraction in the 10% interval was in the 50-94% range in case of pellets with enalapril maleate and in the 52-97% range in case of hydrochlorothiazide pellets. Thus all size distributions can be regarded as good.

4.4.3. Factorial design

The effect of the different process parameters as factors was studied on the basis of a mixed (2 and 3) level full factorial design. The response surfaces of the various optimization parameters may be described with the following general equation:

$$y = b_0 + b_1x_1 + b_2x_2 + b_{22}x_2^2 + b_3x_3 + b_{33}x_3^2 + b_{12}x_1x_2 + b_{13}x_1x_3 + b_{23}x_2x_3 \quad \text{(Eq. 1.)}$$

(where x_1: spheronization time, x_2:liquid feed rate, x_3: spheronization speed)

The regression coefficients and statistical results are displayed in Table 5., significant factors are highlighted with bold numbers.

Table 5.: Effects of factors on the Aspect ratio (AR) and breaking hardness

	AR		Hardness	
	EM	**HCT**	**EM**	**HCT**
R^2	0.9215	0.9525	0.7070	0.7996
MS Residual	0.0047	0.0023	4.1575	3.6379
b_0	**1.283**	**1.285**	**15.515**	**14.370**
b_1	**-0.047**	**-0.080**	**1.764**	**2.002**
b_2	**-0.129**	**-0.117**	**-1.373**	-1.237
b_{22}	**0.071**	0.007	0.434	0.413
b_3	**-0.107**	**-0.099**	0.381	**1.561**
b_{33}	-0.004	0.005	0.104	-0.204
b_1b_2	0.008	-0.031	0.398	-0.782
b_1b_3	-0.014	0.014	0.623	-0.039
b_2b_3	**0.069**	0.030	0.154	0.153

It can be seen from the statistical results that the aspect ratio is significantly influenced by all three factors, within standard 95% CI ($p<0.05$) and the liquid feed rate (x_2) has the most considerable effect, while spheronization time (x_1) has the smallest, for both APIs.

The higher factor values resulted in smaller aspect ratio values and also in the formation of sphere-shaped pellets in both cases. Nevertheless, the considerable difference between the two APIs is that the aspect ratio of HCT pellets decreases linearly with the increment of the liquid addition rate, while EM exhibits a nonlinear dependence on this factor (Fig. 7a, b). The explanation of this difference may be the different solubility of the APIs, which exerts

considerable effect on the pellet texture through the influencing of the distribution of the water inside the wet mass.

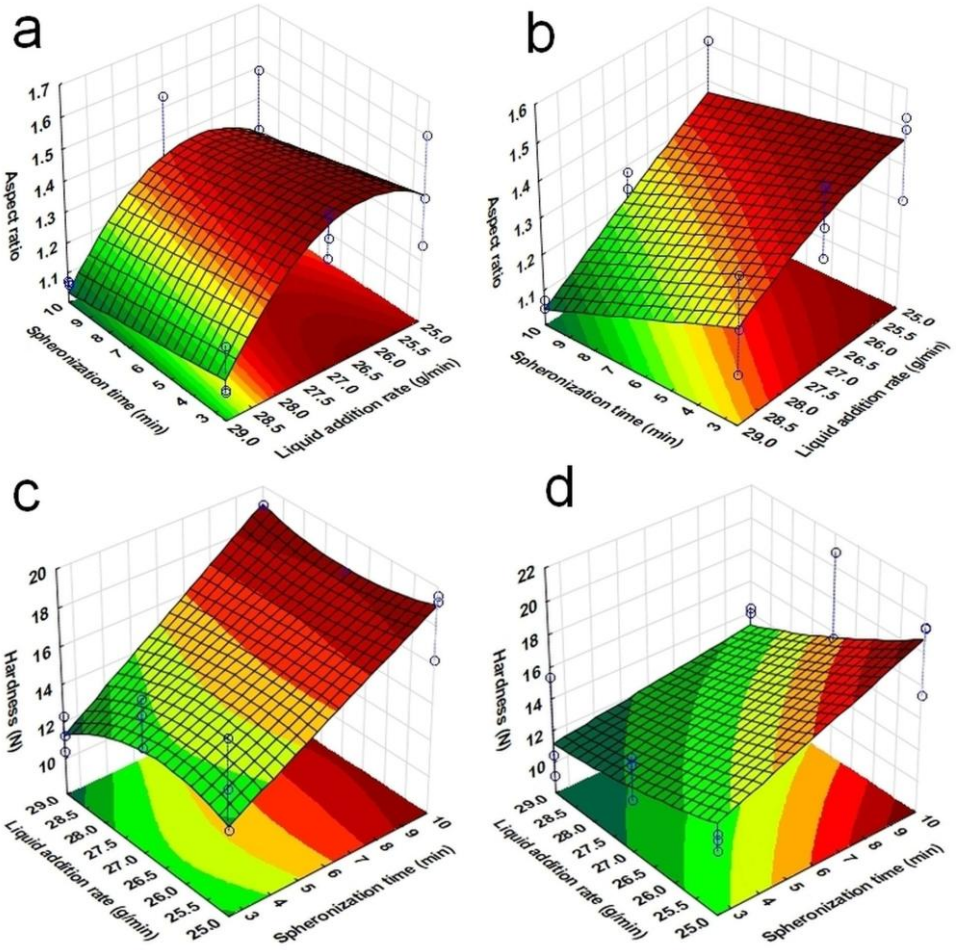

Figure 7.: Response surface on the aspect ratio of EM (a) and HCT (b), and hardness of EM (c) and HCT (d) pellets

The structural differences are well visible on the cross-sectional scanning electron micrographs (Fig. 8.). Although the low magnification images show compact spongiform texture for all investigated samples, the pellets with higher aspect ratio exhibit slightly higher apparent porosity. The increasing magnification reveals the differences of the sponge-like texture of the EC-MCC matrices. Besides the smooth surface of the embedded EM crystals surrounded with fibriform, filamentous, crumpled MCC grains, numerous rounded EC particles connected to them can be clearly identified in EM 1 (x_1, x_2, x_3 = -1), pellets (Fig. 8c). Despite the different embedding mechanism of the API crystals, where the rounded particles are distributed more uniformly in the matrix, the general matrix texture of HCT 1 (x_1, x_2, x_3 = -1) pellets is similar and the round EC grains may be identified (Fig. 8d). The different

embedding can be due to the fact that smaller crystals are bound to the surface with a smaller force than to the matrix formers. The breaking surface of the pellets is generally splintered, which indicates strong cohesion between the particles, but numerous fibrous ruptures may be identified, which can be due to the elastic deformation of the EC grains during the breaking process (Fig. 8g, h).

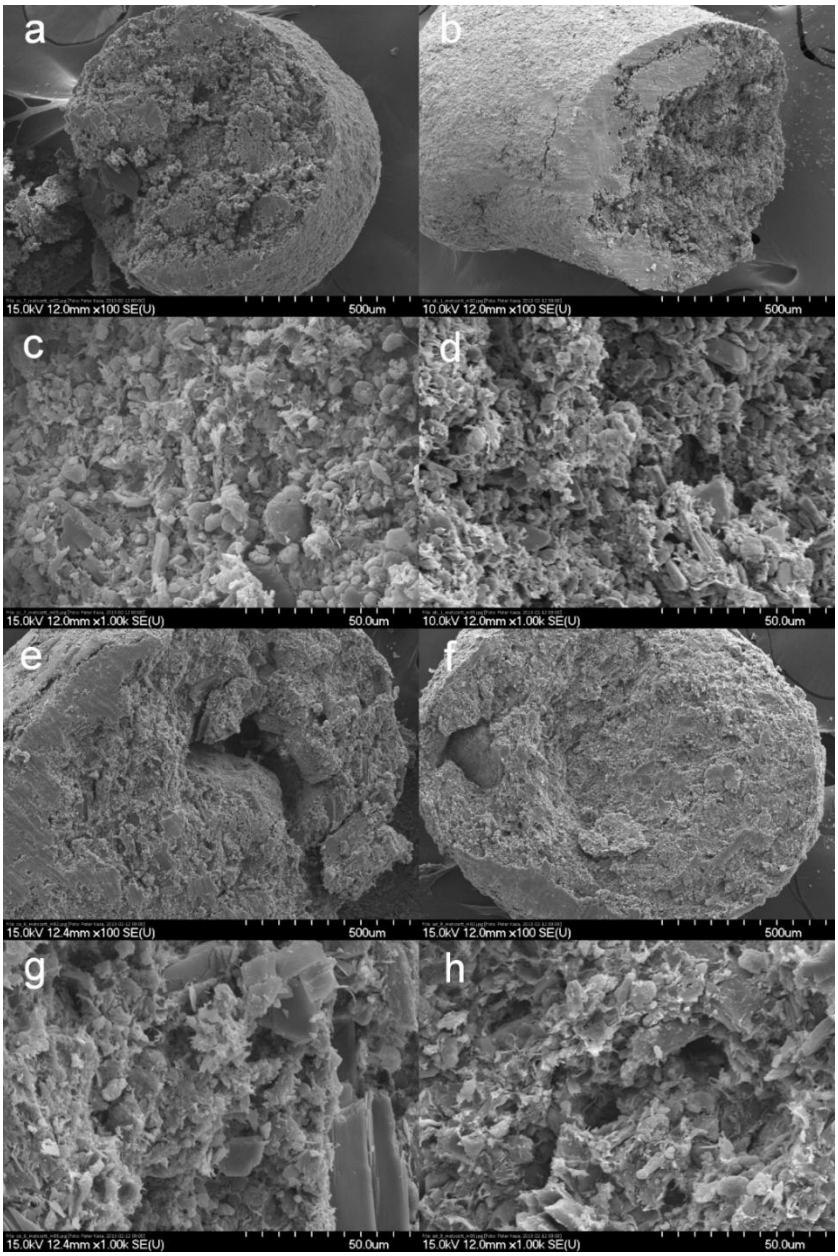

Figure 8.: Scanning electron micrographs of the cross sections of various pellets (EM 1 100x (a), HCT 1 100x (b), EM 1 1000x (c), HCT 1 1000x (d), EM 18 100x (e), HCT 18 100x (f), EM 18 1000x (g), HCT 18 1000x (h))

Consecutively, intact, rounded EC grains cannot be identified in EM 18 and HCT 18 (x_1, x_2, x_3 = +1). This indicates that the high liquid feed rate induced structural changes in EC grains, and the better deformation of these samples may be due to the plasticizing effect of the water. If the better soluble EM bonds more water, that could be the reason for the nonlinear relation between the aspect ratio and liquid addition rate in these pellets.

The differences of the two APIs are also visible if we take into consideration the interactions between the factors. In the case of EM pellets, the interaction of the spheronization speed and the liquid feed rate is significant, and the other interactions have negligible effect. In contrast, the interaction of the liquid feed rate with the two spheronization parameters has equal weight for HCT pellets. In general, the spheronization speed has almost no effect on the shape of the particles at low liquid feed rates, which also supports the negative effect of the unplasticized EC grains on this parameter. The different texture and embedding mechanism of the API crystals have also significant effect on the the mechanical properties (hardness) of pellets.

The maximal breaking strength of HCT pellets is lower in comparison with the corresponding EM ones possibly due to the different embedding and distribution of API particles within the EC-MCC matrix. Furthermore, the statistical analysis revealed that although the pellet hardness is influenced most significantly by spheronization time, within 95% CI ($p<0.05$) for both APIs, but amongst the other factors the liquid feed rate is significant for the EM and the spheronization speed for the HCT pellets (Table 5.). This indicates different behaviour of the various textures, which may be related to the different number and arrangement of solid bridges inside the matrix. The greater hardness of EM pellets is possibly related to the greater amount of dissolved particles due to the better solubility of the API, which results in more intense solid bridge formation after the drying and recrystallization of these particles.

4.4.4. Dissolution

To the dissolution, the pellets were filled together into HPMC capsules (25mg of EM, 10 mg of HCT). The dissolution of the pellets containing hydrochlorothiazide lasts longer than that of pellets containing enalapril maleate (Fig. 9.).

On the basis of dissolution examinations we can prove that the water solubility of the active ingredients significantly influences the dissolution. EC matrix does not inhibit the dissolution of the active ingredient, in case of EM with good dissolution properties (BCSIII). Approximately after 30 minutes, 80% of the acitve ingredient has already dissoluted from the pellets; in this case we cannot talk about sustained/modified release, this could only be

reached by adding more EC to the system. In such case the adding of more EC would be necessary.

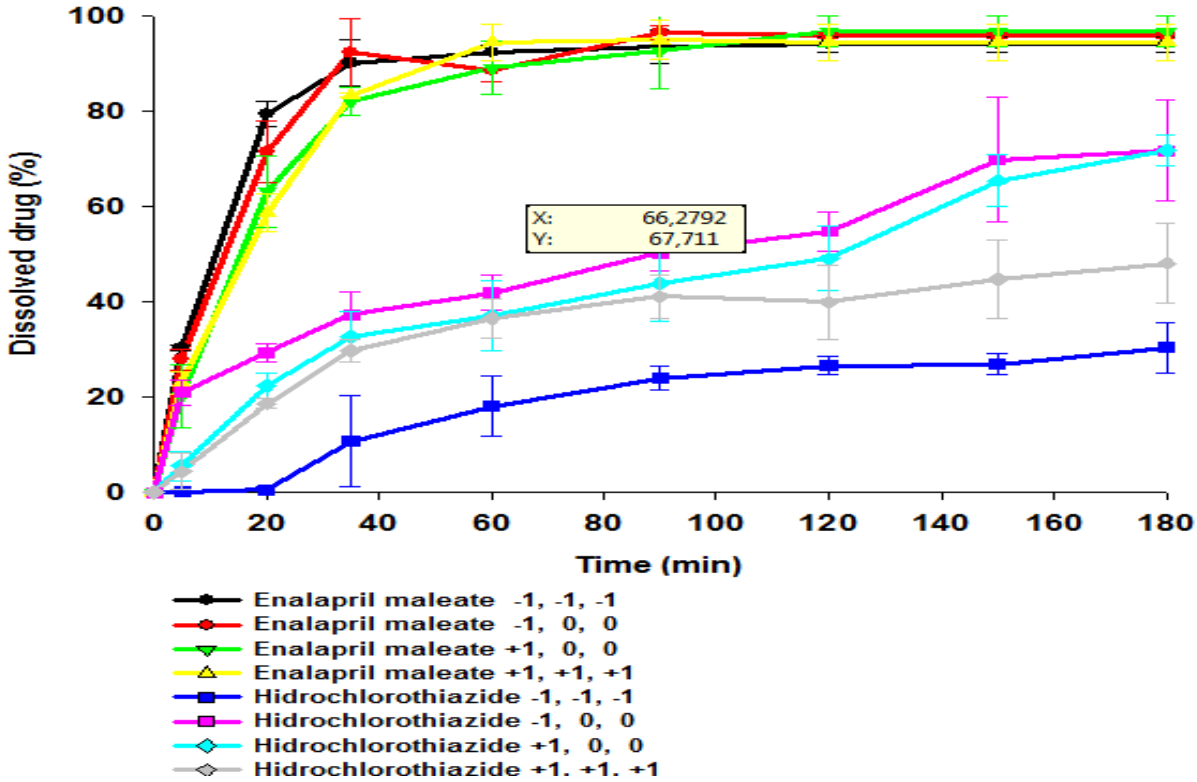

Figure 9.: The disssolution of the pellets

In the case of HCT (BSC IV) with poor dissolution properties, the active ingredient could not dissolute quickly from the matrix, but this was not our goal anyway.

We can see it from the results that by keeping the formulation parameters on a low level, dissolution only begins after a delay period, lag time.

We can determine that spheronization time has a decisive influence on the commencement and degree of the dissolution.The other important parameter is not other than spheronization speed. Spheronization parameters do have a greater influnece in general on dissolution, than the parameters playing role in the formation of the wet mass that is to say liquid feed rate during extrusion.

The results draw our attention to the fact that during the preformulation examinations, in the case of poor water solubility active ingredients, *designing has specific importance*.

5. FINAL CONCLUSIONS, NOVELTY, PRACTICAL USEFULNESS

As previously described in Section: Aims, our goal was to study the application of the widely used ethylcellulose polymer as film forming- and matrix former agent, and with the use of them develop innovative dosage forms with and for combined APIs.

The important novelty and practical usefulness of this work may be summarized as follows:

- Different properties of film forming effects were observed among the used film forming agents and we have come to the conclusion that EC45 has better properties, furthermore we have determined the optimal concentration of plasticizer (triethyl citrate).
- Films with better quality can be prepared from EC45, the prepared films stayed stable until approximately 200°C.
- The results of the FT-IR method supported all the examination data that were gained by other examination methods, such as thermostability and the incorporation of the plasticizer.
- PALS studies showed that 1% plasticizer is integrated between the polymer chains and has greater breaking strength, more concentration of the plasticizer results in larger free volume holes and lower breaking strength.
- Based on the above results, the composition prepared from EC45 polymer with 1% triethyl citrate as plasticizer is recommended for making MR coats. This composition can be used for diffusion coating to obtain a product with modified release.
- With the use of EC and MCC as matrix former, a monolithical matrix system was developed, containing enalapril maleate and hydrochlorothiazide as APIs. We could prepare pellets with optimal physico-chemical properties in both cases. If we want to produce an extended release system, it is essential to know the correct ratio of MCC/EC to achieve monolithic matrix pellets.
- The results of our experiments show that the parameter values and factors influencing extrusion and spheronization depend first of all on the properties of the active ingredient with poor aquos solubility, thus preformulation and detailed planning is essential in the case of poor aquos solubility active ingredients; and furthermore the use of factorial design is essential for their determination.In the case of HCT-pellets, we managed to achive an extended drug release, opposite to EM; but in case of EM-pellets, the addition of more EC may achieve the modified release.

- Capsule dosage forms can be formed with the filling of pellets containing EM and HCT. (In Hungary there are only tablets with these API combination.) The formulation of capsules can be an alternative opportunity for patients with dysphagia, who can gulp capsules easier than tablets.
- The results and observations of the present study provide useful information for industrial technologists.

PUBLICATIONS RELATED TO THE THESIS

I. G. Regdon Jr., **D. Hegyesi**, K. Pintye-Hódi:

Thermal study of ethyl cellulose coating films used for modified release (MR) dosage forms.

J. Therm. Anal. Calorim. 108, 347-352 (2012)

IF (2012): 1,982

II. **D. Hegyesi**, T. Sovány, O. Berkesi, K. Pintye-Hódi, G. Regdon jr.:

Study of effect of plasticizer on the structure and surface characteristics of ethylcellulose free films with FT-IR spectroscopy

Microchemical Journal 110, 36-39 (2013)

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IV. **D. Hegyesi**, M. Thommes, P. Kleinebudde, T. Sovány, P. Kása Jr., A. Kelemen, K. Pintye-Hódi, G. Regdon Jr.:

Preparation and physico-chemical characterization of matrix pellets containing APIs with different solubility via extrusion process.

(manuscript submitted for publication)

PRESENTATIONS RELATED TO THE THESIS

I. **D. Hegyesi**, T. Sovány, O. Berkesi, K. Pintye-Hódi, G. Regdon jr.

Study of the effect of the plasticizer on the structure and surface characteristics of ethylcellulose free films with FT-IR spectroscopy.

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Istanbul, Turkey, 2012.03.19-2012.03.22.

II. **D. Hegyesi**, K. Pintye-Hódi, G. Regdon jr.

Investigation of the thermal behaviour of ethyl cellulose coating films for the purpose of modified release (MR)

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OTHER PRESENTATION

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Investigation of coating processes and of separated polymer films from model solid dosage forms

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