



**BUDAPEST UNIVERSITY OF TECHNOLOGY AND ECONOMICS  
FACULTY OF CHEMICAL ENGINEERING AND BIOENGINEERING  
GEORGE OLAH DOCTORAL SCHOOL**

**Excipient effect on the diffusion of active pharmaceutical ingredients  
through different artificial membranes modelling human and canine  
absorption**

**SUMMARY OF PhD DISSERTATION**

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## INTRODUCTION

The success of generic drug development fundamentally depends on how reliably we can predict, using *in vitro* measurements, the factors and mechanisms that govern gastrointestinal dissolution and permeation, as these processes strongly influence clinical performance and bioequivalence. Improving solubility and permeability therefore remains a central topic in formulation research. However, the prediction of bioequivalence still faces considerable challenges, creating a clear need for predictive, mechanistically grounded, and cost-effective *in vitro* methods.

Over the past decade, several international initiatives have been launched to better characterize gastrointestinal processes and to develop *in vitro* tools with improved clinical relevance. These include the Understanding Gastrointestinal Absorption-related Processes (UNGAP)<sup>1</sup> and Oral Biopharmaceutics Tools (ORBITO)<sup>2</sup> projects supported by the European Union, as well as the FDA's formulation predictive dissolution<sup>3</sup> (fPD) program. Consequently, research efforts have increasingly shifted toward the development of protocols that integrate with existing *in vitro* platforms—such as diffusion cells and combined dissolution–permeation systems—and toward the assessment of their applicability and limitations.

Beyond human biopharmaceutics, increasing attention has been directed toward the dog as an animal model. Few species share such a long evolutionary and cultural history with humans, dating back approximately 12,000 years, and this close biological relationship is reflected in several similarities in gastrointestinal physiology.<sup>4</sup> As a result, the dog has become one of the most important models for studying oral bioavailability and conducting preclinical *in vivo* experiments.<sup>5,6</sup> Today dogs are considered full family members, with their welfare playing an important role in society; more than 500 million dogs live worldwide, and the global veterinary market reached USD 49.96 billion in 2024, with projections of USD 80.85 billion by 2030. At the same time, the use of dogs in *in vivo* studies is increasingly restricted by the 3R principles (Replacement, Reduction, Refinement), as defined in Directive 2010/63/EU<sup>7</sup>, emphasizing both ethical and cost-efficiency considerations and encouraging the replacement of animal experiments with advanced *in vitro* methods whenever possible.

1 CA16205 - European Network on Understanding Gastrointestinal Absorption-Related Processes (UNGAP).

2 Lennernäs, H. et al. Oral Biopharmaceutics Tools - Time for a New Initiative - An Introduction to the IMI Project OrBiTo. *Eur. J. Pharm. Sci.* 2014, 57 (1), 292–299.

3 Hens, B. et al. Formulation Predictive Dissolution (FPD) Testing to Advance Oral Drug Product Development: An Introduction to the US FDA Funded '21st Century BA/BE' Project. *Int. J. Pharm.* 2018, 548 (1), 120–127.

4 Freedman, A. H. et al. Genome Sequencing Highlights the Dynamic Early History of Dogs. *PLoS Genet.* 2014, 10 (1).

5 Lui, C. Y. et al. Comparison of Gastrointestinal PH in Dogs and Humans: Implications on the Use of the Beagle Dog as a Model for Oral Absorption in Humans. *J. Pharm. Sci.* 1986, 75 (3), 271–274.

6 Akimoto, M. et al. Gastric PH Profiles of Beagle Dogs and Their Use as an Alternative to Human Testing. *Eur. J. Pharm. Biopharm.* 2000, 49 (2), 99–102.

7 DIRECTIVE 2010/63/EU OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 22 September 2010 on the Protection of Animals Used for Scientific Purposes.

The need for *in vitro* systems that biorelevantly model the physiological and chemical characteristics of the canine and human gastrointestinal tract arises from the substantial intra- and interspecies variability in gastrointestinal conditions. In dogs, the gastric pH in the fasted state can vary widely, typically between pH 1.5 and 6.8, and increases from pH 6.2 to 7.5 along the small intestine, which can significantly affect the dissolution and absorption of weakly basic and weakly acidic drugs.<sup>8,9</sup> Despite the close physiological relationship between dogs and humans, notable differences remain—including the composition of intestinal fluids, bile salt and phospholipid content, as well as gastric emptying and intestinal transit times—each of which can influence drug dissolution and membrane transport.<sup>9–11</sup> These species-specific differences underscore the need for biorelevant media and protocols tailored to dogs to enable reliable prediction of formulation behaviour.

The most important physicochemical parameters governing oral bioavailability are solubility and permeability. Modern *in vitro* techniques—such as side-by-side diffusion cells and combined dissolution–permeation platforms—enable the simultaneous investigation of these parameters. In recent years, research has increasingly focused on developing protocols that integrate specific membranes and media into existing instruments, allowing small-volume, rapid, discriminative, and biorelevant comparison of formulations, while also supporting the development of *in vitro*–*in vivo* correlations (IVIVC).

This PhD research was carried out within a close collaboration between Pion Inc. (USA), Semmelweis University, the Budapest University of Technology and Economics, and Lavet Pharmaceuticals Ltd. Pion Inc. provided state-of-the-art *in vitro* equipment for simultaneous dissolution–permeation studies; the two universities contributed scientific background for mechanistic interpretation and IVIVC assessment; while Lavet Ltd. offered industrial expertise in veterinary formulation development.

**One** of the **central aims** of this dissertation was to deepen the mechanistic understanding of key physicochemical parameters, with particular emphasis on how excipients (such as cyclodextrins, surfactants, and pH modifiers) and hydrodynamic conditions (stirring and the unstirred water layer) influence apparent permeability and flux across lipophilic and size-exclusion membranes. A **second major objective** was the development of small-volume, simple discriminative and canine-relevant, *in vitro* dissolution–permeation protocols suitable for the ranking and comparison of formulations, as well as for predicting bioequivalence in veterinary drug development.

8 Kararli, T. T. Comparison of the Gastrointestinal Anatomy, Physiology, and Biochemistry of Humans and Commonly Used Laboratory Animals. *Biopharm. Drug Dispos.* 1995, 16 (5), 351–380. <https://doi.org/10.1002/bdd.2510160502>.

9 Dressman, J. B. Comparison of Canine and Human Gastrointestinal Physiology. *Pharmaceutical Research: An Official Journal of the American Association of Pharmaceutical Scientists*. 1986, pp 123–131. <https://doi.org/10.1023/A:1016353705970>.

10 Sjögren, E. et al. *In Vivo Methods for Drug Absorption - Comparative Physiologies, Model Selection, Correlations with in Vitro Methods (IVIVC), and Applications for Formulation/API/Excipient Characterization Including Food Effects*; 2014; Vol. 57. <https://doi.org/10.1016/j.ejps.2014.02.010>.

11 USP. <1236> USP Solubility Measurements. *United States Pharmacopoeia* 2021, *USP 43–NF*, 1–13.

## METHODS

### *Investigation of the Limiting Step of Membrane Transport*

Transport across lipophilic and size-exclusion membranes was measured using the MicroFLUX™ small-volume dissolution–permeation system (Pion Inc.) under various pH conditions and stirring rates. Using physicochemical derivations and calculations, I determined whether the rate-limiting step of transport was the passage of the drug across the membrane or transport through the unstirred water layer.

### *Equilibrium Solubility Studies/ Phase-solubility studies*

An excess amount of the drug substance was added to the selected media, and the resulting suspension was stirred for 6 hours and then allowed to settle for 18 hours. The concentration of the dissolved drug in the liquid phase was determined in situ using UV-probe.

### *Transport of HP- $\beta$ -CD Across Membranes*

The transport of HP- $\beta$ -CD across lipophilic membranes (PVDF sheets impregnated with *n*-dodecane) and size-exclusion membranes (1 kDa and 6 kDa MWCO) was investigated using the MicroFLUX™ system, which consists of donor and acceptor cells separated by an artificial membrane. The appearance of HP- $\beta$ -CD in the acceptor phase was detected via its complexation with phenolphthalein, monitored by UV-probe.

### *Small-Volume Simultaneous Dissolution–Permeation Studies*

Simultaneous dissolution–permeation experiments were conducted using the MicroFLUX™ system (Pion Inc.). The instrument contains 20 mL donor and 20 mL acceptor chambers, separated by an artificial membrane (PVDF, 1.54 cm<sup>2</sup>) impregnated with *n*-dodecane or a GIT-lipid mixture.

### *High-Throughput Permeability (PAMPA)*

Solutions containing the drug and excipients at specified concentrations were pipetted into the donor compartment simulating the gastrointestinal tract, while the acceptor compartment contained pH 7.4 phosphate buffer representing the bloodstream. The two compartments were separated by a membrane impregnated with a GIT-lipid mixture.

### *Dissolution Testing*

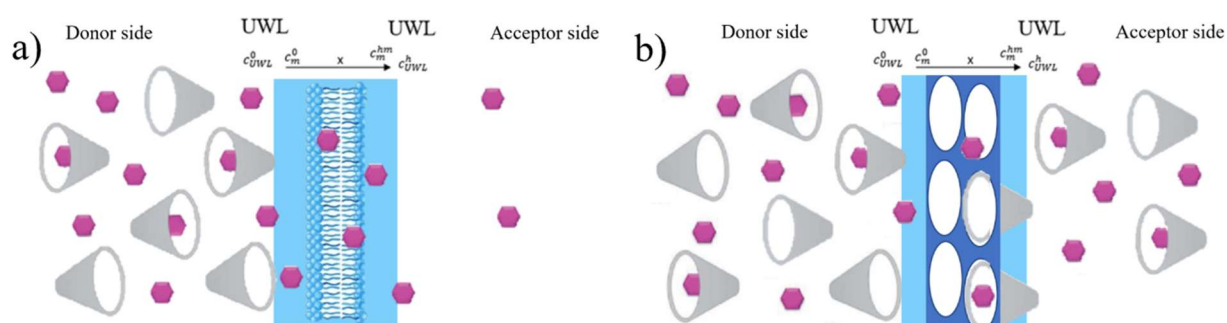
Dissolution studies were performed using a USP II apparatus with 1000 mL dissolution medium, at 37 °C and 75 rpm. Samples were withdrawn at 10, 20, 30, and 45 minutes, and drug concentrations were quantified using HPLC.

## RESULTS

The first part of the dissertation investigates the impact of donor-side HP- $\beta$ -CD on the dissolution–permeation behaviour of carvedilol across lipophilic and size-exclusion membranes, with particular emphasis on the role of stirring intensity, the driving force of transport, and the applicability of the concentration-based mathematical model derived from Fick’s first equation. The second part explores how sink conditions manifest differently depending on membrane type. The third part demonstrates the importance of early, combined solubility and permeability assessment, using pimobendan as a model compound, and highlights the pronounced effects of solubilizing and pH-modifying excipients. In addition, small-volume biorelevant and discriminative dissolution–permeation protocols suitable for formulation ranking and quality control were developed.

In the first part of the dissertation, the dissolution–permeation behaviour of carvedilol across lipophilic and size-exclusion membranes was investigated at pH 10 in UWL (Unstirred Water Layer) limited case at different stirring speeds in the presence and absence of HP- $\beta$ -CD on the donor side. As a solubilizing agent HP- $\beta$ -CD was used. Phase-solubility studies confirmed that both polymorphic forms of carvedilol form a stable 1:1 complex with HP- $\beta$ -CD, resulting in a threefold increase in solubility, establishing cyclodextrin as a suitable model excipient for subsequent experiments.

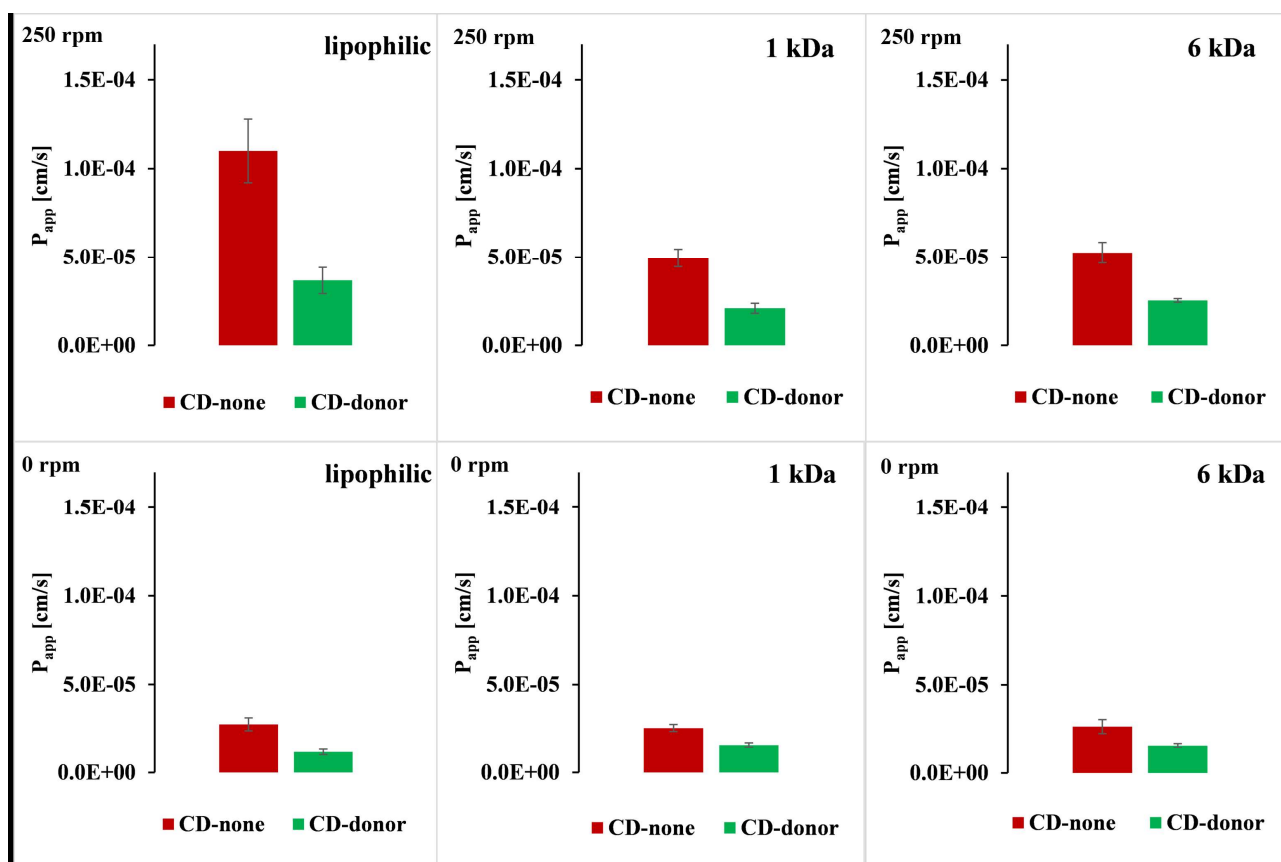
The transport of API and the drug-cyclodextrin complex was investigated through three different membrane types: lipophilic, and 1 kDa and 6 kDa (MWCO) size-exclusion membranes, Leading to fundamentally different transport mechanisms: the lipophilic membrane allowed only the free drug to permeate, whereas both the drug, HP- $\beta$ -CD and their complex permeated across the 1 kDa and 6 kDa membranes. (**Figure 1.**)



**Figure 1.** Schematic drawing of membrane transport in case of a) lipophilic membrane b) size-exclusion membrane (API is represented with pink hexagons, while the cyclodextrin is with grey cones)

The statistical analysis of the apparent permeability ( $P_{app}$ ) values calculated from the studies conducted at 250 rpm and 0 rpm stirring, with and without cyclodextrin as a solubilizing excipient, using a three-factor ANOVA, showed that all three examined factors – membrane type, stirring speed, and

the presence of the solubilizing excipient – had a significant effect on the apparent permeability ( $P_{app}$ ). The application of stirring (250 rpm) resulted in a significant increase in permeability in all cases, whereas in the absence of stirring, due to the effect of the thick, unstirred aqueous layer, the apparent permeability values measured across the three membranes were nearly identical. (Figure 2)

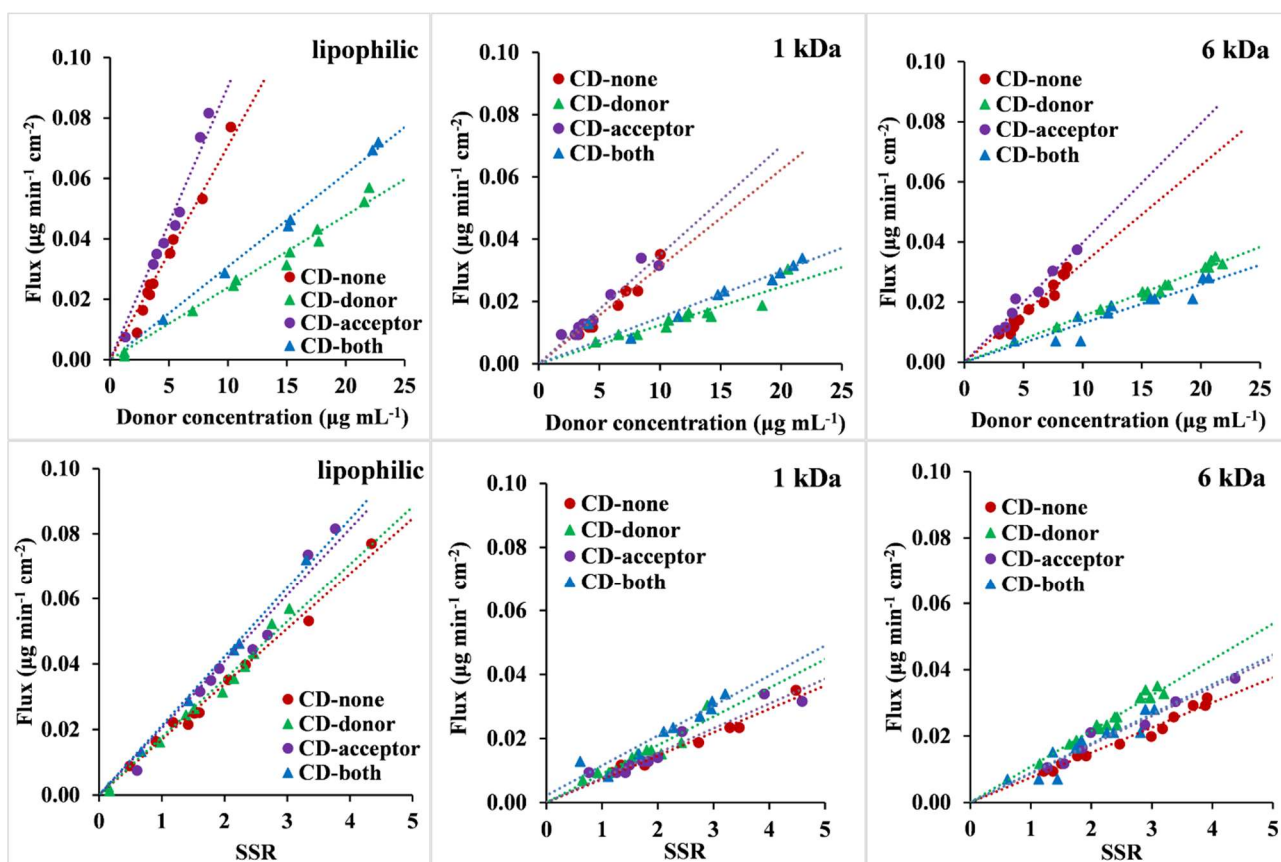


**Figure 2.** Apparent permeability values at pH 10, with stirring speed 250 rpm and 0 rpm, lipophilic, 6 kDa and 1 kDa size-exclusion membrane in the absence of HP- $\beta$ -CD (CD-none), and in the presence of HP- $\beta$ -CD in the donor compartment (CD-donor)

Based on the obtained data, I determined the membrane permeability ( $P_m$ ) characteristic of the lipophilic membrane and the thickness of the unstirred water layer (hUWL), which exceeded 2000  $\mu\text{m}$  in the absence of stirring, while with intensive stirring it fell within the range of 70–360  $\mu\text{m}$ .

Furthermore, it can be observed that under appropriate stirring conditions, the presence of HP- $\beta$ -CD in the donor solution significantly reduces permeability across both the lipophilic and size-exclusion membranes. This clearly confirms the inverse relationship between solubility and permeability; however, this effect can only be reliably evaluated under sufficient stirring (250 rpm). These results demonstrate that the solubility–permeability interplay can be observed in the same manner for both membrane types, and that the intensity of stirring plays a key role in revealing the permeability-modifying effects of formulation excipients.

In the second part of the thesis, we discuss the case where the solubilizing excipient is added either to the acceptor side or to both sides of the membrane in a well-stirred system (250 rpm) under pH 10 conditions. The flux–donor concentration curves (**Figure 3**) show that the highest flux values were measured when HP- $\beta$ -CD was placed on the acceptor side, thereby creating sink conditions, in combination with a lipophilic membrane. In contrast, switching to size-exclusion membranes or applying the cyclodextrin on the donor side resulted in a significant decrease in flux. It is clearly visible from the flux–donor concentration diagrams that the addition of the solubilizing excipient to the system (to either or both compartments) affects the slope of the curves, which is a factor proportional to permeability.



**Figure 3.** Flux - donor concentration and flux - SSR curves in pH 10 buffer with 250 rpm stirring rate for lipophilic membrane, 1 kDa, and 6 kDa size-exclusion membranes. No HP- $\beta$ -CD present on either side of the membrane with **red** called ‘**CD-none**’, addition of HP- $\beta$ -CD to acceptor side with **purple** called ‘**CD-acceptor**’, addition of HP- $\beta$ -CD to donor side with **green** called ‘**CD-donor**’ and addition of HP- $\beta$ -CD to both side with **blue** called ‘**CD-both**’

Using physico-chemical equations, I derived a concentration-based mathematical model suitable for describing transport through a membrane valid in UWL limited case, in which the driving force of transport can be described by the supersaturation ratio (SSR) on the donor and acceptor sides:

$$J = B_e \left( \frac{c_D}{c_D^*} - \frac{c_A}{c_A^*} \right) \quad \text{Eq.1}$$

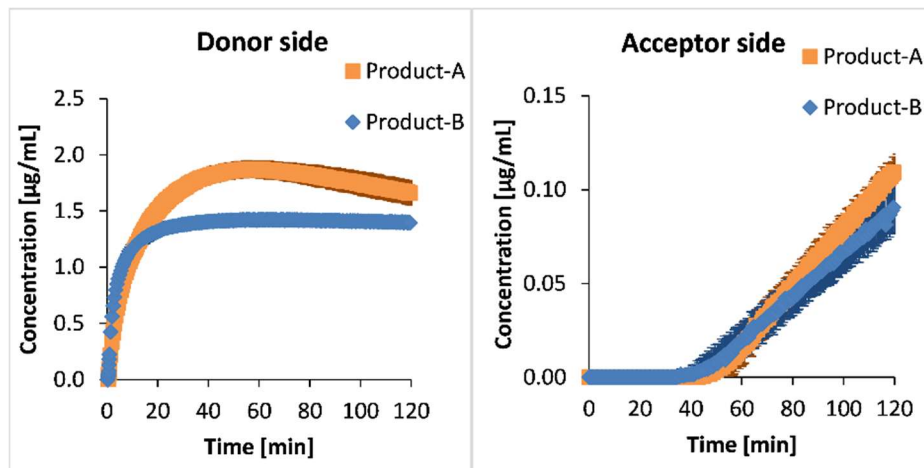
Where  $J$  is the flux,  $c_D$  and  $c_A$  are the drug concentrations on the donor and acceptor sides, respectively, and the values marked with an asterisk represent equilibrium solubility.  $B_e$  is the effective

proportionality factor, which describes the combined effect of diffusion through the unstirred water layer (UWL) and the membrane.

From the equation, it is evident that solubility — a factor dependent on the solubilizing excipient— appears in the variable term. The flux–supersaturation curves obtained at 250 rpm stirring (Figure 3) show that the data measured on the lipophilic and 1 kDa membranes fit the model well, as parallel straight lines were obtained. The presence of cyclodextrin on the donor side only affects transport if CD is able to pass through the membrane (as in the case of the 6 kDa size-exclusion membrane). In contrast, the presence of CD on the acceptor side resulted in a true sink effect in the case of the lipophilic membrane, which led to an increase in the slope — that is, the  $B_e$  value. On the other hand, with size-exclusion membranes, the passage of CD through the membrane practically eliminated the sink effect, and the flux-SSR lines remained parallel.

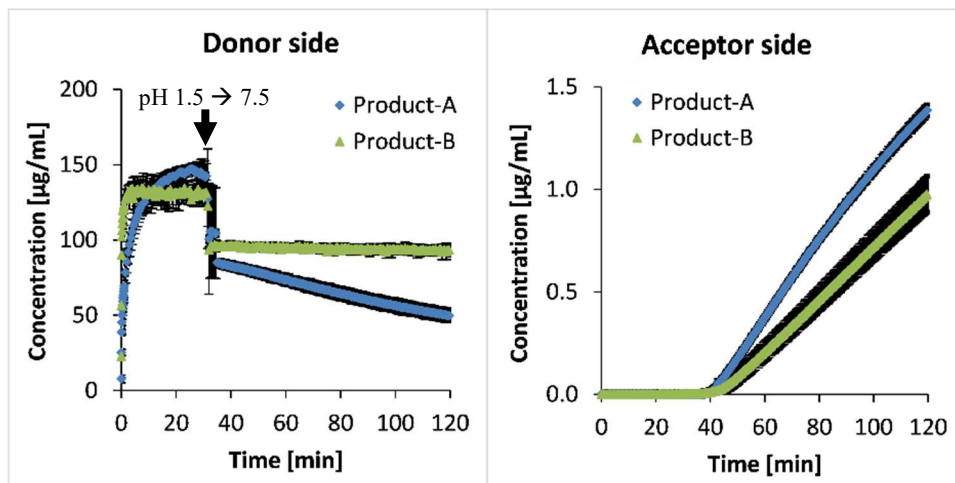
The third part of the dissertation demonstrated that the solubility and permeability of pimobendan are strongly dependent on pH and excipient composition, which fundamentally determines bioavailability. Based on the pH-solubility profile, pimobendan exhibits orders-of-magnitude higher solubility at low pH. Equilibrium solubility and PAMPA measurements revealed that different additives—surfactants and pH-modifiers—enhance solubility to varying extents and may simultaneously decrease effective permeability, illustrating the solubility–permeability interplay.

A pH 4.5 medium, representing the canine proximal small intestine, proved discriminative for comparing the dissolution of different formulations. Small-volume MicroFLUX™ studies at pH 4.5 (**Figure 4.**) showed that although neither formulation reached the target donor concentration of 5 µg/mL, Product-A produced higher donor concentrations and a steeper acceptor-side profile, resulting in higher flux. This was consistent with the PAMPA results, where in the presence of malic-acid PIMO showed reduced permeability, while Macrogol 6000 and Gelucire did not reduce permeability. Bioequivalence calculations using log-transformation, showed that the 90% confidence interval of flux values remained within the 80–125% acceptance range, demonstrating that the method is suitable for predicting bioequivalence.



**Figure 4.** Concentration curves at donor and acceptor side in case of Product-A and Product-B formulation with pH 4.5 discriminative donor buffer

Beyond the discriminative QC compatible protocol, three types of biorelevant protocol with pH-shift, simulating canine gastric and intestinal fluids was also developed. Among the conditions tested, the pH 1.5 → pH 7.5 transition best reflected the bioequivalence of the two products. Even in this biorelevant system, the pH-modifier-containing Product-B showed slightly reduced flux (**Figure 5.**), but the difference was not significant, and the 90% confidence interval again remained within the 80–125% range.



**Figure 5.** *In vitro* side-by-side diffusion cell assay results measured using the developed method with biologically relevant pH change on the donor side (pH 1,5 – pH 7,5)

## THESIS FINDINGS

1. Comparing the lipophilic membranes (PVDF plates impregnated with *n*-dodecane), which are generally used to model drug permeation and size-exclusion membranes (regenerated cellulose), an inverse relationship between solubility and permeability was observed for both membrane types: when a solubilizing excipient was introduced into the donor phase, the solubility of the active pharmaceutical ingredient increased, whereas its apparent permeability decreased. It was also established that adequate stirring is indispensable for evaluating the effects of formulation excipients on permeability, since in both membrane systems the influence of solubilizing agents on permeability was significantly reduced under non-stirred conditions compared to stirred experiments [I].
2. It was established that in a three-layer system consisting of an unstirred water layer – membrane – unstirred water layer, the driving force of transport cannot be simplified to the concentration difference between the donor and acceptor phases, when a solubilizing excipient affecting the drug's solubility is also present in the system. This is valid for both the membrane-limited and the unstirred water layer-limited conditions. The driving force of transport can be instead be described by the difference in supersaturation ratio between the two sides of the membrane. This relationship was mathematically derived from Fick's first law for membranes that allow only the drug to permeate, while the excipient and the drug–excipient complex cannot pass through. The validity of this concentration-based mathematical model was experimentally confirmed using lipophilic as well as 1 kDa cut-off size-exclusion membranes in a carvedilol–HP- $\beta$ -CD system, where the excipient was placed in the donor phase [I].
3. Under sink conditions, where the solubilizing excipient was placed in the acceptor phase, it was confirmed that the concentration-based mathematical model of transport is applicable for the three-layer system consisting of the membrane and the unstirred liquid layers formed on its surface. For the lipophilic membrane, it was demonstrated that the presence of cyclodextrin in the acceptor compartment not only influenced the driving force of carvedilol transport by increasing its solubility, but also altered the apparent thickness of the unstirred water layer. In contrast, for size-exclusion membranes, the presence of cyclodextrin in the acceptor phase had no significant effect on the rate of transport. [II]
4. It was confirmed that the concentration-based mathematical model of transport through the three-layer system consisting of the membrane and the unstirred water layers formed on its surface is also applicable when cyclodextrin is present on both sides of membrane. In this case, the hydrodynamic size of the solubilizing excipient allows it to permeate through the membrane; however, due to the absence of a concentration gradient, the extent of excipient transport is negligible (6 kDa cut-off size-exclusion membrane), while the permeation of carvedilol remains dominant. [II]
5. Small-volume (20 mL) simultaneous dissolution–permeation studies were applied to compare originator and generic veterinary formulations containing pimobendan for the first time. The originator product contained surfactants, whereas the generic formulation included pH-modifying agents. The effects of these excipients on the solubility and permeability of the active pharmaceutical ingredient were investigated. The experimental results confirmed an inverse relationship between solubility and permeability at pH 4.5 in the donor media. Based on bioequivalence calculations using logarithmic transformation, the 90% confidence interval of the flux measurements remained within the acceptance range (80–125%), indicating that the method proved to be suitable for determining the bioequivalence of these formulations. [III]

## APPLICATION OF THE RESULTS

The results of the present dissertation clearly demonstrate that the key physicochemical processes governing the oral absorption of poorly water-soluble drugs — dissolution, supersaturation and precipitation, and permeation across the intestinal barrier — can only be reliably described using *in vitro* methods that capture these processes simultaneously. The small-volume dissolution–permeation systems developed and mechanistically evaluated in this work serve this purpose, with particular emphasis on modeling the canine gastrointestinal environment, which is a key preclinical model both in human drug development and in the formulation of veterinary medicines.

The comparison of lipophilic and size-exclusion membranes provided deeper insight into how formulation excipients such as cyclodextrins modify transport mechanisms and how the driving force changes under sink and non-sink conditions. The significance of the concentration-based mathematical model lies in its ability to quantitatively describe membrane transport in the presence of solubilizing agents, thereby offering a rational framework for the optimization of formulation design. The mathematical description of the transport processes across lipophilic and size-exclusion membranes presented in this thesis will, in the future, enable the design of experimental setups using size-exclusion membranes in cases where lipophilic membranes are not stable over the measurement period (e.g., in the case of liposomes), thereby providing an alternative method of measurement.

The pimobendan studies highlighted that the quality and quantity of excipients fundamentally influence solubility and permeability, making their early, targeted evaluation essential for designing appropriate bioavailability. The developed simple simultaneous dissolution–absorption protocol, which is easy to use even in quality control and capable of detecting small differences between formulations, has since been adopted in the industry. To demonstrate good *in vitro*–*in vivo* correlation of the protocols involving biorelevant pH shifts, future studies will need to test formulations of active pharmaceutical ingredients with varying acid–base characteristics (weak acids, weak bases, neutral or even zwitterionic compounds). The application of biorelevant pH-shift protocols demonstrated that—under carefully controlled experimental conditions—simultaneous dissolution–permeation assays are capable of predicting bioequivalence *in vitro*, thus contributing to the reduction of costly and ethically sensitive *in vivo* studies.

Overall, this dissertation establishes a methodological framework that substantially supports both generic and innovative drug development, particularly in the challenging field of poorly soluble active pharmaceutical ingredients.

## PUBLICATIONS

### Related scientific articles

- [I] **Tózsér, P.**; Kovács, L.L.; Kádár, Sz.; Csicsák, D.; Sóti, P.; Völgyi, G.; Sinkó B.; Borbás, E.; Nagy, Z. K.; The effect of surfactants and pH modifying agents on the dissolution and permeation of Pimobendan. *Periodica Polytechnica Chemical Engineering*, **2023**. <https://doi.org/10.3311/PPch.20970> IF: 1.3 Q3
- [II] **Tózsér, P.**; Kádár, Sz.; Szabó, E.; Dobó, M.; Tóth, G.; Balogh, Gy.T.; Sóti P.; Sinkó, B.; Borbás, E.; Comparison of lipophilic and size-exclusion membranes: the effect of stirring and cyclodextrin in the donor compartment. *ADMET and DMPK*, **2025**. 13(4), 2753. <https://doi.org/10.5599/admet.2753> IF: 4.3 Q1
- [III] **Tózsér, P.**; Kádár, Sz.; Szabó, E.; Pataki, H.; Sóti, P.; Laczay, P.; Balogh, Gy.T.; Sinkó, B.; Borbás, E.; Comparison of lipophilic and size-exclusion membranes: creating sink condition with cyclodextrin. *ADMET and DMPK*, **2025**. 13(5), 2859. <https://doi.org/10.5599/admet.2859> IF: 4.3 Q1

### Further articles

- Borbás, E.; **Tózsér, P.**; Tsinman, K.; Tsinman, O.; Takács-Novák, K.; Völgyi, G.; Sinkó, B.; Nagy, Z. K. Effect of Formulation Additives on Drug Transport through Size-Exclusion Membranes. *Mol. Pharm.* **2018**, 15, 3308-3317, IF: 4.396 Q1
- Csicsák, D.; Borbás, E.; Kádár, Sz.; **Tózsér, P.**; Bagi, P.; Pataki, H.; Sinkó, B.; Takács-Novák, K.; Völgyi, G. Towards more accurate solubility measurements with real time monitoring: a carvedilol case study. *New J. Chem.* **2021**, 45, 11618, IF: 3.591 Q2
- Kádár, Sz.; **Tózsér, P.**; Nagy, B.; Farkas, A.; Nagy, Z. K.; Tsinman, O.; Tsinman, K.; Csicsák, D.; Völgyi, G.; Takács-Novák, K.; Borbás, E.; Sinkó, B.; Flux-Based Formulation Development—A Proof of Concept Study. *AAPS J.* **2022**, 24:22, IF: 4.5 Q1
- Kádár, Sz.; Csicsák, D.; **Tózsér, P.**; Farkas, A.; Pála, T.; Mirzahosseini, A.; Tóth, B.; Tóth, G.; Fiser, B.; Horváth, P.; Madarász, J.; Avdeef, A.; Takács-Novák, K.; Sinkó, B.; Borbás, E.; Völgyi, G.; Understanding the pH Dependence of Supersaturation State—A Case Study of Telmisartan. *Pharmaceutics*. **2022**, 14, 1635, IF: 5.4 Q1
- Csicsák, D.; Szolláth, R.; Kádár, S.; Ambrus, R.; Bartos, C.; Balogh, E.; Antal, I.; Köteles, I.; **Tózsér, P.**; Bárdos, V.; Horváth, P.; Borbás, E.; Takács-Novák, K.; Sinkó, B.; Völgyi, G.; The Effect of the Particle Size Reduction on the Biorelevant Solubility and Dissolution of Poorly Soluble Drugs with Different Acid-Base Character. *Pharmaceutics*. **2023**, 15, 278. IF: 6.525 Q1

- Kádár, Sz.; Kennedy, A.; Lee, S.; Ruiz, R.; Farkas, A.; **Tózsér, P.**; Csicsák, D.; Tóth, G.; Sinkó, B.; Borbás, E.; Bioequivalence prediction with small-scale biphasic dissolution and simultaneous dissolution-permeation apparatus—An aripiprazole case study. *EUR J PHARM SCI.* 198 **2024**, 106782, IF: 4.3 Q1
- Bárdos, V.; Szolláth, R.; **Tózsér, P.**; Mirzahosseini, A.; Sinkó, B.; Angi, R.; Takács-Novák, K. Study of the Influence of Pharmaceutical Excipients on the Solubility and Permeability of BCS Class II Drugs. *Sci. Pharm.* **2025**, 93(2), 19. IF: 2.5 Q2

### Presentations

- **Tózsér Petra**; Borbás Enikő; Sinkó Bálint; Takácsné Novák Krisztina; Völgyi Gergely; Konstantin Tsinmann; Marosi György; Nagy Zsombor Kristóf; *Méretkizárásos membrán, mint a lipid membránok alternatívája*, XII. Szent-Györgyi Albert Konferencia, **2018**, Budapest (Prezentáció)
- **Tózsér Petra**; Borbás Enikő; Sinkó Bálint; Takácsné Novák Krisztina; Völgyi Gergely; Konstantin Tsinmann; Marosi György; Nagy Zsombor Kristóf; *Méretkizárásos membrán mint a lipidmembránok alternatívája*, XLII. Kémiai Előadói Napok, **2019**, Szeged (Prezentáció)
- **Tózsér Petra**; Jaksáné Borbás Enikő; Sinkó Bálint; Takácsné Novák Krisztina; Völgyi Gergely; Konstantin Tsinmann; Marosi György; Nagy Zsombor Kristóf; *In situ kinetikai oldhatóság mérés UV-szonda segítségével*, XLIII. Kémiai Előadói Napok, **2020**, Szeged (Prezentáció)
- **Tózsér Petra**; Gyáfrás Lilla Vivien; Jaksáné Borbás Enikő; Sinkó Bálint; Nagy Zsombor Kristóf; *Karvedilol-ciklodextrin komplex kioldódás-felszívódás vizsgálata*, XLIV. Kémiai Előadói Napok, **2021**, Szeged (Prezentáció)
- **Tózsér Petra**; Kovács Luca Lili; Kádár Szabina; Csicsák Dóra; Sóti Péter; Völgyi Gergely; Nagy Zsombor K.; Borbás Enikő; Sinkó Bálint; *The effect of surfactants and pH modifying agents on the dissolution and permeation of Pimobendan*, AAPS PharmSci 360, **2022**, Boston, MA (Poszter)
- **Tózsér Petra**; Kovács Luca Lili; Kádár Szabina; Csicsák Dóra; Sóti Péter; Völgyi Gergely; Sinkó Bálint; Nagy Zsombor K.; Jaksáné Borbás Enikő; *Felületaktív anyagok és pH-módosító segédanyagok hatása a pimobendán kioldódására és felszívódására*, XLVI. Kémiai Előadói Napok, **2023**, Szeged (Prezentáció)