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Investigations of mass transfer in simulated biomedical systems

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Abstract
The work motivation was to investigate *in vitro* system simulating drug release from Drug Eluting Stent (DES). The experiments were conducted in a custom designed unit simulating drug release from polymer covering DES in a simplified way. The active substance diffuses from a thin, internal annular layer of hydrogel (imitating "stent") to the outer cylindrical layer of hydrogel ("artery wall") and is at once drifted away by coaxially flowing solution ("blood"). The conducted research proved functionality of the experimental unit. The rate of mass transfer depends considerably on the mass driving force and on the affinity of substance-hydrogel. The volumetric flow rate and liquid viscosity did not affect the process significantly. The effective diffusion coefficient was calculated as a process parameter and then used in the other variants. Diffusion in hydrogel is the mechanism limiting the mass transfer in the examined system. For the first attempt, the diffusive model used in literature was employed. The provided calculations are consistent with experimental data and therefore show that despite its simplifications the model allows to estimate the amount of released substance. In conclusion, the relative substance mass, changing over time, was estimated in the respective parts of the unit. The prospect of determining the relative mass of the substance appearing in the subsequent parts of the system over time provides the opportunity to adjust the respective process parameters, which will facilitate control over the rate of mass release.

Keywords
diffusion, biomedical system, stent, modelling, mass transfer

1. INTRODUCTION

Drug release in biomedical systems is a multi-stage, complex process. The interdisciplinary outlook incorporating physical and biochemical phenomena, mathematical modelling and experimental verification would allow better understanding of mechanisms governing these processes.

Atherosclerosis seems to be one of the most common and, at the same time, the most dangerous illnesses of our times. Coronary artery disease leads to the narrowing of blood vessels by atherosclerotic plaque, which can result in myocardial infraction. One of the most effective methods of the disease's treatment is to expand the artery by implanting inside the blood vessel a stent, i.e. a cylindrical metal element that acts as a scaffolding. Previously used Bare Metal Stents (BMS) frequently led to an irritation of the blood vessel walls during the implantation. This often caused restenosis, which is the excessive production of endothelial cells, and finally resulted in the re-narrowing of the blood vessel artery (Pietrasik and Rdzanek, 2017). This issue was resolved by the invention of the second generation of stents, the so-called Drug Eluting Stents (DES), which are covered by polymers that release antiproliferative drugs. The third generation of stents are Biodegradable Stents, which seem very promising, as they should degrade after serving their function. Their applicability is widely tested (Ilnicka et al., 2009).

The problems discussed in the literature focus on different aspects of the process. We will shortly mention only a few of them to underline how complex and multidisciplinary the problem is.

The properties of the stent scaffolding were considered in terms of the suitability of different materials, the stent surface and mechanical properties, the stent-tissue interactions, and type of material covering the scaffolding, e.g. in (Mani et al., 2007). The influence of different types of DES designs (especially of the weave-like pattern design) on the stent-induced blood flow disturbances as well as on the concentration of the eluted drug at the artery wall was investigated in (Seo et al., 2016). The selection of appropriate polymers was also examined: several types of polymers were used as coating for a stent (Kamberi et al., 2009). Different types of polymers were used for the *in vitro* drug release simulation from a stent (Semmling et al., 2014). Different types of solutions were examined as blood replacements in *in vitro* studies, imitating drug release from stent system in (Khan et al., 2013).

Going back to the subject of this work, we would like to mention only a few methods of *in vitro* experimental studies, which simulated drug release from a stent. The simplest and therefore popular approach was to immerse the examine stent carrying active substance in a proper solution (usually PBS pH 7,4) and apply intensive, thermostatic shaking (Guo et al., 2009; Khan et al., 2013). The obtained solution was

analyzed and exchanged at predetermined times. Usually, the whole procedure took about two or three months. However, an "accelerated" method was also developed and presented in (Kamberi et al., 2009). The abovementioned procedures did not simulate the mechanism, yet they were easy and simple to refer to.

The vessel-simulating flow-through cell (vFTC) method for the *in vitro* evaluation of substance release and distribution from drug-eluting stents was developed and tested in (Neubert et al., 2008). A stent coated with the model substance was mounted inside the central lumen of the cylindrical, hydrogel compartment (made of agarose, polyacrylamide or polyvinyl alcohol). The fluid flowed throughout the central aperture. The experiments allowed to estimate the specific contributions of the substance present in the respective parts of the system. The aim of the study was to check the influence of hydrophobic additives added to the "artery wall" on substance release. The further investigations of other related factors were continued e.g. in (Seidlitz et al., 2015).

The paper (O'Brien et al., 2011) showed another original experimental setup, containing a small stripe, made of fluorescein-loaded polyurethane elastomer, mimicking a single stent strut. The stripe was mounted in the poly-vinyl alcohol-based hydrogel as a model tissue bed, with the fluid flowing in the hydrogel lumen. The analysis of the substance distribution was conducted with an epifluorescent microscope. The influence of pulsatile blood flow on arterial drug deposition has been investigated by the same research team in (O'Brien et al., 2013; Vijayaratnam et al., 2018).

The aim of all the abovementioned works was the same: to refine the most effective stent system, which would result in a therapeutically effective drug concentration in the artery vessel tissue, together with a small systemic release. Therefore, the methods of controlled drug release, and the data on the percentage of the drug absorbed by the artery wall versus the amount of the active substance diluted in the blood flow, are objects of interest for the scientists.

The purpose of his work was to investigate the system which would, in a very simplified way, imitate drug release from the drug eluting stent. In the process, the active substance located in the polymer is migrating by diffusion to the artery wall tissue, while being simultaneously drifted away by the convection of the flowing blood. The idea of the proposed unit conformation was inspired by previously mentioned works, especially (Neubert et al., 2008; O'Brien et al., 2011).

2. EXPERIMENTS

The performed experiments simulated systems where the active substance diffuses from the thin layer to the outer, annular part of hydrogel, and is simultaneously drifted away by the convection of the liquid.

The measurements were conducted in the original system (Fig. 1a), with the custom designed experimental "Flow Unit" (Fig. 1b). The coaxial, thin, internal hydrogel collet, containing an active substance simulated a "stent". The central aperture formed a cylindrical lumen with "blood" flowing in a closed loop (simulated by water or water with the additive of sodium salt of carboxymethyl cellulose CMC-Na), while the external, cylindrical collet made of hydrogel (biological agar) simulated the "artery wall". Different experiment variants were performed differing flowrates, kind of active substances and their initial concentrations and liquid viscosities (Kopka, 2023; Turula, 2023).

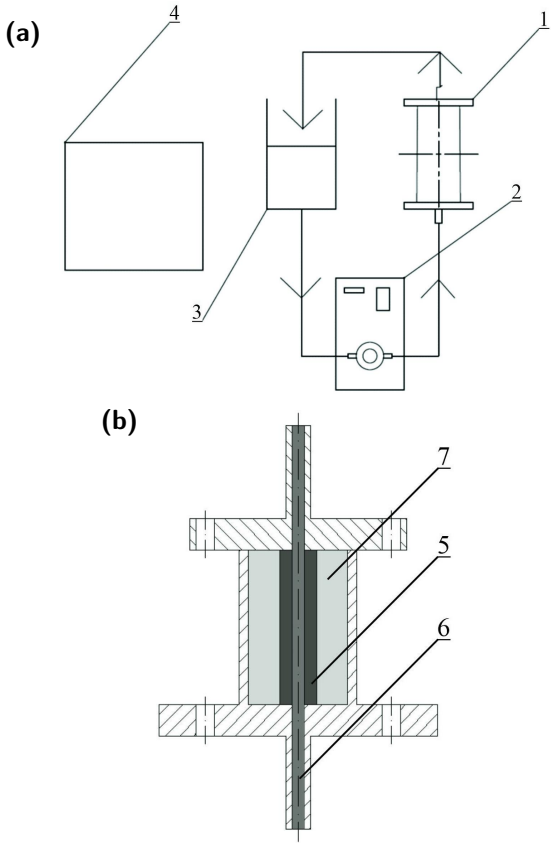

Figure 1. (a) Scheme of the experimental system (Weber, 2020): Flow Unit (1), pomp Ismatec IP65 (2), liquid reservoir (3), spectrophotometer Hitachi UV Vis U-2900 (4); (b) Scheme of the Flow Unit (Turula, 2023): inner collet hydrogel with active substance imitating a "stent" (5), solution flowing in a closed loop simulating "blood" (6), hydrogel (biological agar) simulating an "artery wall" (7).

All the experiments were conducted following the procedure described below. At first, the agar solution was prepared taking the proportions: 1 g agar per 17.75 g water. The ingredients were mixed with heating for about 45 minutes to obtain a clear, homogeneous liquid. The fluid was poured into the outer annular volume of Flow Unit (the inner part was then separated by the specially fabricated divider) and left to cool and solidify for about 24 hours. After 24 hours, analogously,

the agar solution with the additive of the appropriate amount of active substance was prepared and poured into the inner annular volume of Flow Unit (the inner part was then filled with the special, coaxial pivot) and left to cool and solidify for about 1 hour. Meanwhile, water cleaned by the reverse osmosis or the solution of sodium salt of carboxymethyl cellulose was prepared (the volume of the liquid was 200 ml). Afterwards, the coaxial pivot was removed and the Flow Unit was assembled and sealed by tightening the screws. Then, the whole system was connected (Fig. 1a): Flow Unit, pomp, liquid reservoir. At the moment, when water started to flow through the central aperture, the measurements begun. The solution samples were probed from reservoir at determined periods of time and the concentration in the liquid was determined spectrophotometrically. Absorbency was converted into the substance concentration based on calibration curves obtained in previous research. The experiments usually lasted for about 5 hours. Additionally, after the test, the inner part of hydrogel (imitating "stent") was separated. The amount of active substance in this compartment was determined with the use of static desorption method (e.g. sequential shaking of hydrogel in the purified water in a vortex mixer for at least 24 hours).

For these "first attempt" experiments, biological agar was used as the hydrogel simulating "artery walls" as well as "stent coating". This simplification allowed to take into account the same effective diffusion coefficient for both hydrogel parts of the unit (internal hydrogel simulating "stent" and external, cylindrical hydrogel collet imitating "artery wall") and also to reduce the complexity of calculations. The use of different materials for mimicking "stent" and "artery wall" undoubtedly would affect the obtained results, especially in the context of diffusion rate and substance-media affinity. Therefore, in the future researche, various media will be used to simulate "stent" and "artery wall", and their effective diffusion coefficients will be determined in independent tests.

The active substances, chosen due to their similarity to several drug molecules (e.g. molecular weight and size) and their appropriability for spectrophotometric analysis, were: New Coccine, Rhodamine B, Dopamine and Protein standard. The active ingredient initial concentrations varied in the range of: $C_{0S} = 0.01 \div 0.2\%_{\text{mass}}$, consistent with pharmaceutical content.

The flowrate scope ranging $Q = 13 \div 768$ ml/min imitated the values of blood flow in arteries. The viscosity of the liquid was changed by the addition of sodium salt of carboxymethyl cellulose (CMC-Na) in the amount of 0.1% or 0.2% of the solution mass. The values of viscosity were approximately: $4 \cdot 10^{-3}$ Pa·s and $2 \cdot 10^{-2}$ Pa·s, respectively.

3. ANALYSIS OF THE RESULTS

The rates of the mass transfer calculated for the investigated system depended on a variant, and varied in the range of $N'_A = 10^{-10} \div 10^{-7}$ mol/s, which corresponds to the literature values. A few figures below show how individual, investigated factors affected the mass transfer in the considered system (Kopka, 2023).

The higher initial concentration of the substance in the system resulted in the bigger driving force of the process, which caused more intensive transport of the substance (Fig. 2).

The flowrates of the solution were researched within the wide range of values (13÷768 ml/min), corresponding to the

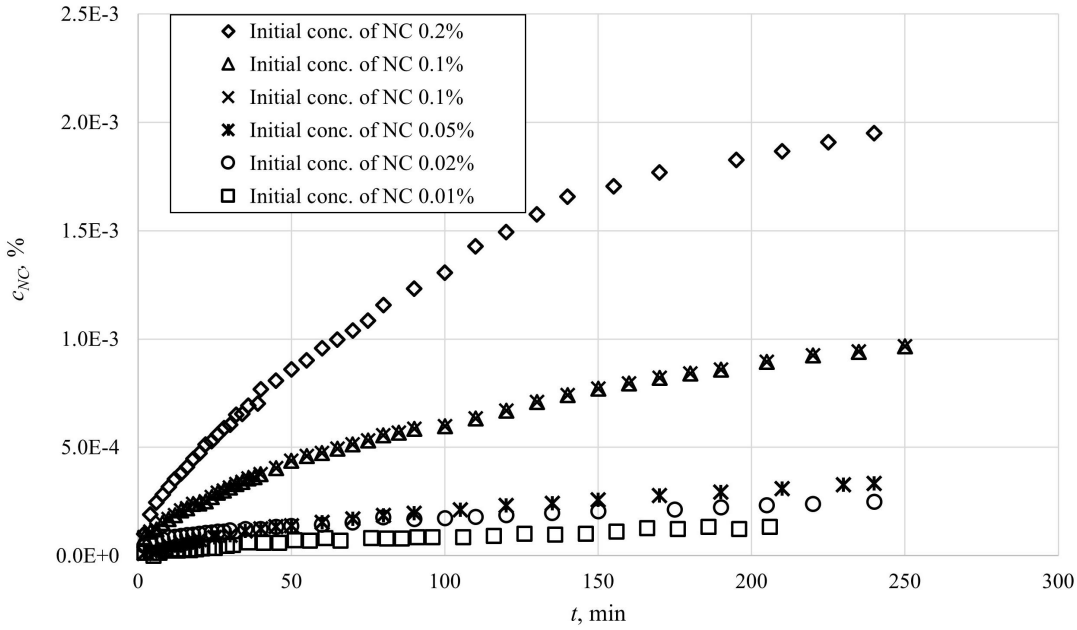

Figure 2. The changes of New Coccine concentration in liquid over time, for variants with different initial concentrations of New Coccine in inner hydrogel ("stent"), flowrate $Q = 30$ ml/min.

magnitudes of blood flow in different cases. The impact of the varying flowrates is not so significant (Fig. 3), which confirms that the diffusion in hydrogel is limiting the mass transfer in this system. The first measurements of the effect of the pulsating flow did not show much impact either, but it has to be reexamined in further research.

The viscosity of the liquid, changed by the addition of 0.1% or 0.2%$_{mass}$ of carboxymethyl cellulose sodium salt, took the approximate values: $4 \cdot 10^{-3}$ Pa·s and $2 \cdot 10^{-2}$ Pa·s, respectively. Nevertheless, the increase of the solution viscosity did not affect the rate of mass release (Fig. 4). This confirmed the diffusion in hydrogel to be the crucial mechanism in this system. This trend was predictable, as the majority of correlations for convection in laminar regime operate on Peclet number, which is independent of viscosity.

The mass transfer of different substances varies meaningfully (Fig. 5). This attests that the size and the steric hindrance of the molecule, and in tandem, the drug's affinity to the polymer and the tissue, are very important factors affecting the drug release.

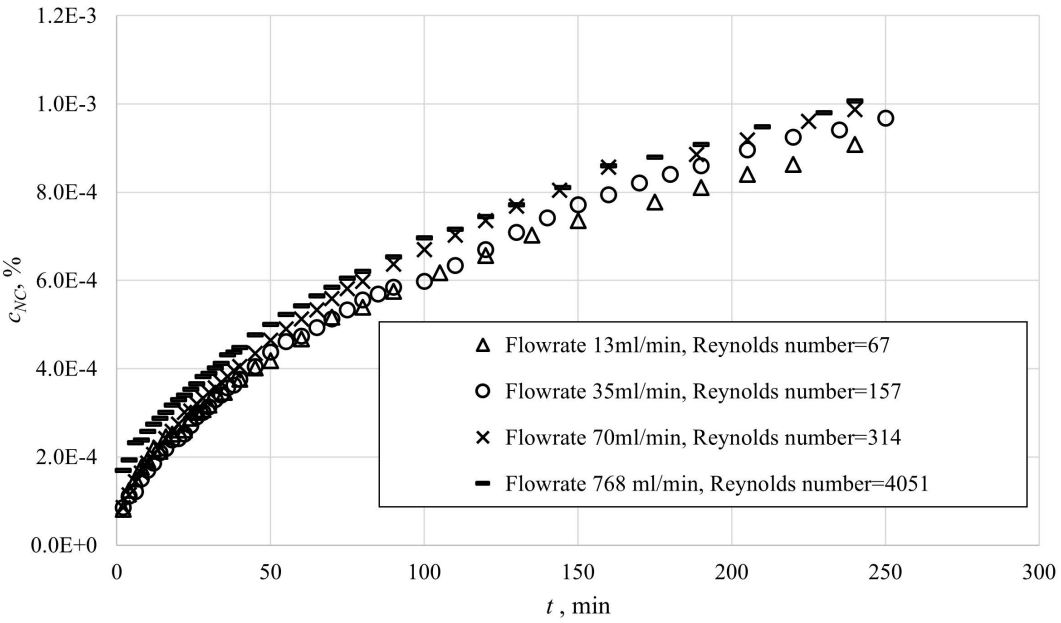

Figure 3. The changes of New Coccine concentration in liquid over time, for different flowrates of solution ("blood"), initial concentrations of New Coccine in the inner hydrogel $C_{0\,NC} = 0.1\%$.

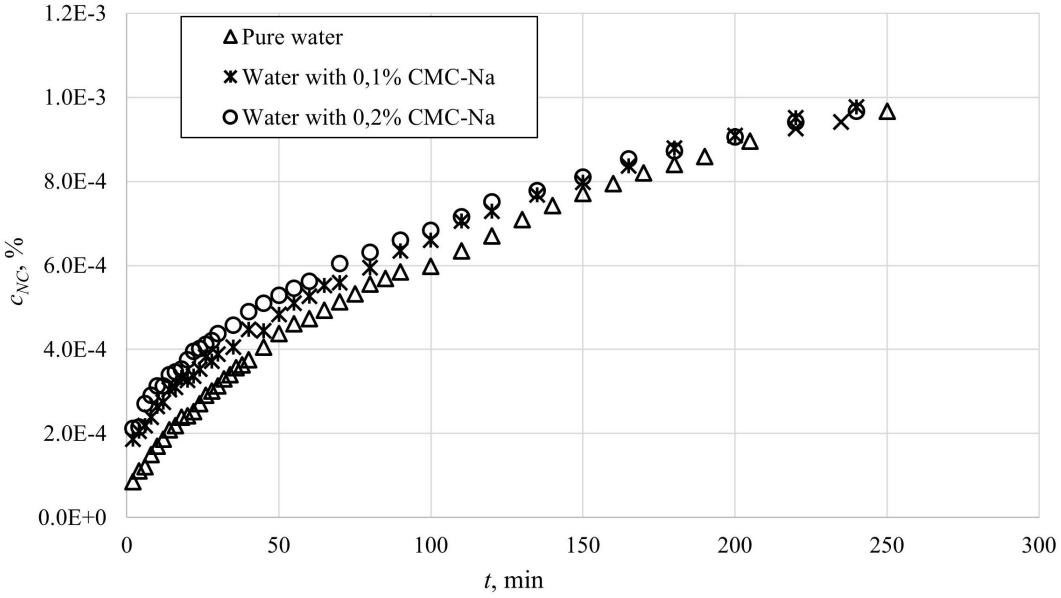

Figure 4. The changes of New Coccine concentration in liquid over time, for variants with different viscosity of the solution ("blood"), initial concentrations of New Coccine in inner hydrogel $C_{0\,NC} = 0.1\%$, flowrate $Q = 30$ ml/min.

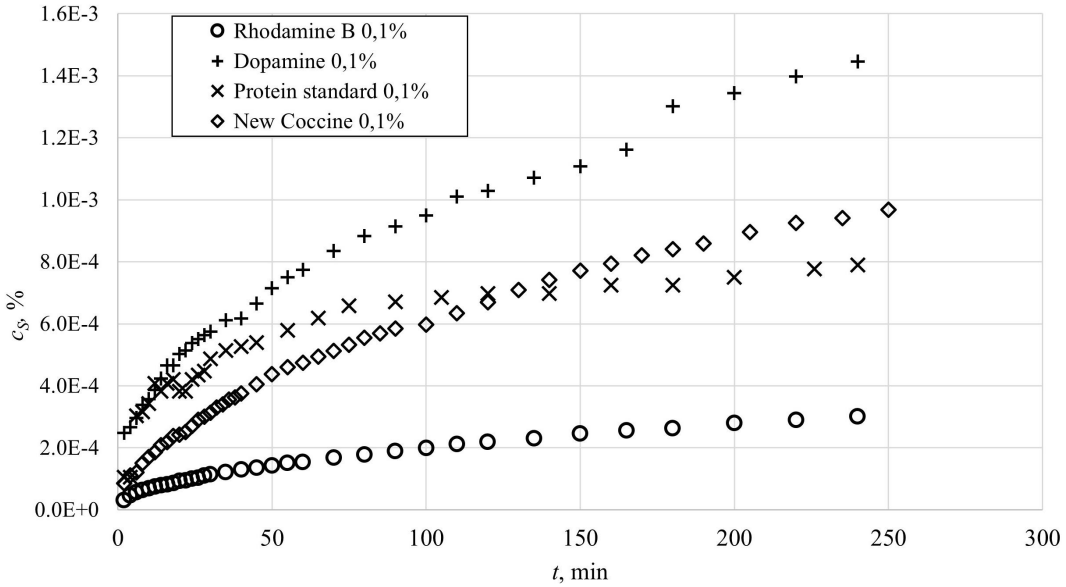

Figure 5. The changes of substance concentration in liquid over time, initial concentrations of substance in inner hydrogel $C_{0S} = 0.1\%$, flowrate $Q = 30$ ml/min.

During the experiments, only the substance concentration in flowing liquid could be continuously measured in time. Therefore, after the experiment, the mass of the rest of the active substance contained in the inner hydrogel ("stent") was determined with the use of static desorption method. As a result, by using mass balance, the amount of substance which migrated to the outer hydrogel ("artery wall") could also be calculated. In Table 1, the substance mass in the respective parts of the system is shown for sample variants.

The results showed that a large amount of the substance is being carried away to the flowing liquid, which means that a significant amount of the drug is not working therapeutically in the designated compartment. The data indicated that the substance mass released to the "artery wall" differs a lot due to the concentration of active substance and type of chemical compound. The relative decrease of the substance fraction diffusing into the "tissue" compartment relies on the slow mass transfer, limiting the diffusion to the outer hydrogel.

4. MASS TRANSFER

The effective diffusion coefficients for different substances were calculated as process parameters, using a fitting method for the basic experiment with the initial concentration of $0.1\%_{\text{mass}}$ and flowrate of 30 ml/min. The obtained values, e.g. for New Coccine $D_{\text{NC,H}} = 4,59 \cdot 10^{-11}$ m^2/s, are consistent with the data obtained in other works (Makowski, 2023; Weber, 2019). The calculated coefficients were then used for the other variants of the experiment. In prospective work, the effective diffusion coefficients will be determined by independent experiments.

The mathematical modelling of the substance release from hydrogel is described by the second Fick's law and proper initial and boundary conditions (Crank, 1975; Crank et al., 1981), (Saltzman, 2001). The transient diffusion of drug from a thin polymer layer, which does not swell or degrade, is given by the formulation:

$$\frac{\partial C_S}{\partial t} = \frac{D_{S,H}\partial^2 C_S}{\partial x^2} \tag{1}$$

Table 1. The substance mass in the respective parts of the system, flowrate $Q = 30$ ml/min, results after 240 minutes of measurement (Kopka, 2023).

Variant	Mass of substance, g		
	in "blood"	in "stent"	in "artery wall"
$C_{0\,\text{NC}} = 0.05\%_{mass.}$	$6.67 \cdot 10^{-4}$	$5.48 \cdot 10^{-4}$	$6.30 \cdot 10^{-3}$
$C_{0\,\text{NC}} = 0.1\%_{mass.}$	$1.93 \cdot 10^{-3}$	$1.43 \cdot 10^{-3}$	$3.80 \cdot 10^{-4}$
$C_{0\,\text{NC}} = 0.2\%_{mass.}$	$3.90 \cdot 10^{-3}$	$3.00 \cdot 10^{-3}$	$5.37 \cdot 10^{-4}$
$C_{0\,\text{NC}} = 0.1\%_{\text{mass}}$., solution with 0.1% CMC-Na	$1.95 \cdot 10^{-3}$	$1.48 \cdot 10^{-3}$	$3.80 \cdot 10^{-4}$
$C_{0\,\text{RB}} = 0.1\%_{mass.}$	$6.01 \cdot 10^{-4}$	$8.14 \cdot 10^{-4}$	$2.30 \cdot 10^{-3}$

Initial and boundary conditions for the above problem take the following formulae:

$$C_S\left(t=0,-\frac{L}{2}<x<\frac{L}{2}\right)=C_{S0} \quad (2)$$

$$\frac{\partial C_S}{\partial x}(t>0,x=0)=0 \quad (3)$$

$$C_S\left(t>0,x=\pm\frac{L}{2}\right)=0 \quad (4)$$

Although the model is simplified, this approach frequently appears in the literature e.g. (Guo et al., 2009; Seidlitz et al., 2011; Semmling et al., 2014; Siepmann and Peppas, 2012). Therefore, just as in previous approach, this diffusive model was applied also in this work. The solution provides two analytical equations of relative mass release from the hydrogel layer presented in (Crank, 1975; Mullarney et al., 2006; Siepmann and Peppas, 2001):

$$f(t)=\frac{m_S(t)}{m_{S0}}= 4\left(\frac{D_{S,H}t}{L^2}\right)^{\frac{1}{2}}\left\{\pi^{-\frac{1}{2}}+2\sum_{n=1}^{\infty}(-1)^n \operatorname{ierfc}\frac{nL}{2\sqrt{D_{S,H}t}}\right\} \quad (5)$$

$$f(t)=\frac{m_S(t)}{m_{S0}}= 1-\sum_{n=0}^{\infty}\frac{8}{(2n+1)^2\pi^2}\exp\left[\frac{-D_{S,H}(2n+1)^2\pi^2 t}{L^2}\right] \quad (6)$$

The above equations can be simplified.

- As the second term in the second brackets of Equation (5) vanishes at short times, a sufficiently accurate approximation of Eq. (3) for $f(t)<0.60$, called an "early-time" approximation can be written as follows (Siepmann and Peppas, 2001):

$$f(t)=\frac{m_S(t)}{m_{S0}}=4\left(\frac{D_{S,H}t}{\pi L^2}\right)^{0.5}$$
$$f(t)=\frac{m_S(t)}{m_{S0}}=2\left(\frac{D_{S,H}t}{\pi L^2}\right)^{0.5} \quad (7)$$

- Similarly, when $f(t)>0.60$, a "late-time" approximation can be derived from Equation (6), which can be simplified to the form (Mullarney et al., 2006):

$$f(t)=\frac{m_S(t)}{m_{S0}}=1-\frac{8}{\pi^2}\exp\left[\frac{-D_{S,H}\pi^2 t}{L^2}\right]$$
$$f(t)=\frac{m_S(t)}{m_{S0}}=1-\frac{8}{\pi^2}\exp\left[\frac{-D_{S,H}\pi^2 t}{4L^2}\right] \quad (8)$$

In the examined system, the distribution of the active substance between three media is considered. Based on the experimental data, we are able to determine the substance mass in the solution ("blood") at a given instance of time and the substance mass in the respective parts of the system, but only at the end of experiment (see Table 1). However, by calculating the substance mass released from the internal hydrogel ("stent") depicted in the model above, it is possible to obtain the substance mass which diffused into the outer hydrogel ("artery wall") at any given instance of time, following the mass balance below:

$$m_S(t)=m_{S\_Artery}(t)+m_{S\_Blood}(t) \quad (9)$$

The values of the relative mass loss of different substances released from the "stent" determined by the experiments were compared with the results obtained from the mathematical model and presented in Table 2.

The values of the relative mass loss of substances determined by the experiments, and the results of calculations obtained from the mathematical model are quite close. The results show that the applied diffusive model, while simplified, can be used to estimate the amount of released substance from the inner hydrogel ("stent").

By using mass balance, it is possible to evaluate the substance mass in the individual parts of the system during any given instance of time of the experiment:

$$m_{S0}=m_{S\_Artery}(t)+m_{S\_Blood}(t)+m_{S\_Stent} \quad (10)$$

The sample distribution of the substance mass in the respective parts of the system over time is shown in Fig. 6.

Table 2. The relative substance mass in percentages in the inner hydrogel ("stent"), the flowrate $Q=30$ ml/min, the results after 240 minutes of experiments.

Variant	Relative mass of substance released from the inner hydrogel ("stent") [%]	
	Experimental data	Calculated value
Variant $C_{0\,NC}=0.05\%_{mass}$	70.3%	60.7%
Variant $C_{0\,NC}=0.1\%_{mass}$	61.8%	61.8%
Variant $C_{0\,NC}=0.2\%_{mass}$	59.7%	60.7 %
Variant $C_{0\,NC}=0.1\%_{mass}+0.1\%$ CMC	61.2%	61.2%
Variant $C_{0\,RB}=0.1\%_{mass}$	78.1%	78.2 %

The literature sources indicated the diffusion as mass transfer limiting stage in such systems. However, to confirm this statement, the convective mass transfer coefficients and hypothetical convective mass flux were calculated for different variants. Below, the scheme of calculations is presented. The regime of the liquid flow was found by calculating Reynolds number:

$$\mathrm{Re} = \frac{\rho \cdot v \cdot d}{\mu} \tag{11}$$

Schmidt number was obtained with the following definition:

$$\mathrm{Sc} = \frac{\mu}{\rho \cdot D} \tag{12}$$

For the laminar flow, as the condition $\mathrm{Re} \cdot \mathrm{Sc} \cdot \frac{d}{L} > 13$ was fulfilled, the following correlation (Eq. 13) describing mass transfer was used.

$$\mathrm{Sh} = 1.62 \cdot \left(\mathrm{Re} \cdot \mathrm{Sc} \cdot \frac{d}{h}\right)^{\frac{1}{3}} \tag{13}$$

Where Sherwood number was given by the formula:

$$\mathrm{Sh} = \frac{k_L \cdot d}{D} \tag{14}$$

Then, the convective mass transfer coefficient was determined:

$$k_L = \frac{D}{d} \cdot 1.62 \cdot \left(\mathrm{Re} \cdot \mathrm{Sc} \cdot \frac{d}{h}\right)^{\frac{1}{3}} \tag{15}$$

The convective mass flux of substance was calculated from Equation (16).

$$N'_A = k_L \cdot \Delta C_r \cdot F \tag{16}$$

Finally, the mass of substance drifted away by convection was obtained from Equation (17).

$$\Delta m_{\mathrm{S\,CONV}} = N'_A \cdot t \cdot M_{\mathrm{S}} \tag{17}$$

The calculated values for the sample experiment are shown below, in Table 3. The results proved that in this system, diffusion in hydrogel limited the rate of the drug release.

Table 3. The sample calculations for the hypothetical situation, where convection is limiting the mass transfer in the examined system, the flowrate $Q = 30$ ml/min, the results after 240 minutes of experiment.

$\mathrm{Re} = \frac{vd\rho}{\mu}$	Pe	Sh	k_L [m/s]	N'_A [mol/s]	$\Delta m_{\mathrm{S\,CONV}} / \Delta m_{\mathrm{S\,EXP}}$
157	$3.16 \cdot 10^3$	$1.02 \cdot 10^1$	$1.28 \cdot 10^{-4}$	$1.16 \cdot 10^{-7}$	250

The obtained ratio of the mass hypothetically transported by convection juxtaposed with the experimentally obtained data results is nonsensical. This supports the claim that the diffusion is the slowest mechanism of mass transfer in this system and therefore it limits the mass release.

5. CONCLUSIONS

- The experiments were conducted in the original, custom designed experimental "Flow Unit", which simulated a biomedical system. The active substance diffused from the thin, internal annular layer (internal hydrogel imitating a "stent") to the outer cylindrical annular layer (hydrogel imitating an "artery wall"), while was simultaneously

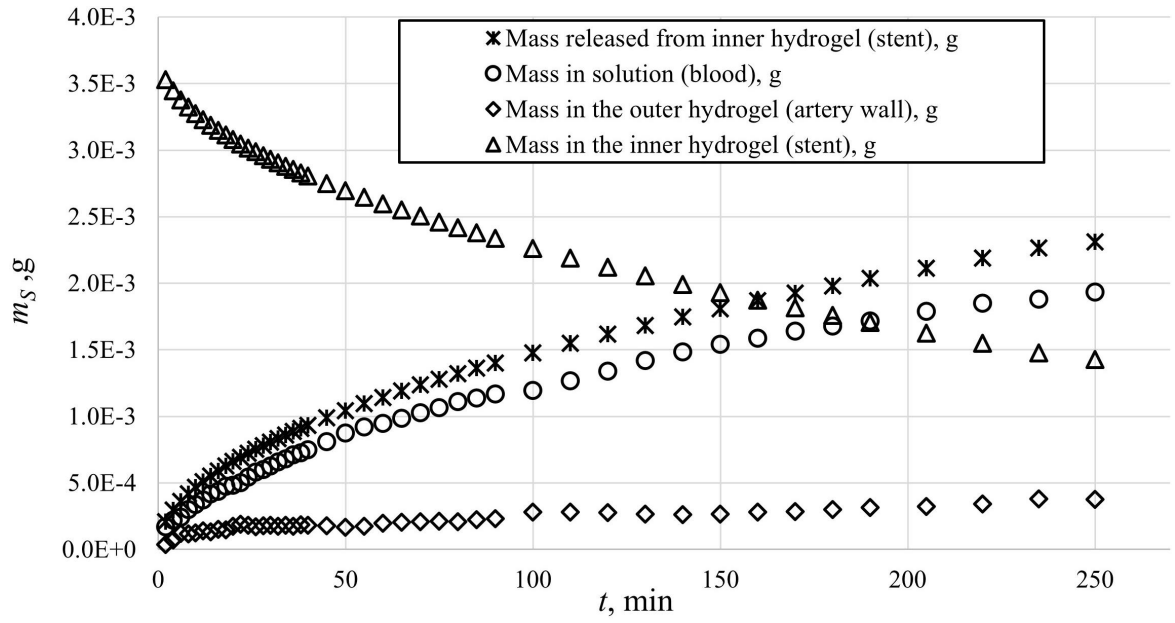

Figure 6. The changes of the substance mass in the respective parts of the system over time, initial concentrations of New Coccine in the inner hydrogel $C_{0\,\mathrm{NC}} = 0.1\%$, flowrate $Q = 30$ ml/min.

drifted away by the coaxially flowing solution (imitating "blood"). The conducted experiments proved the functionality of the "Flow Unit" to simulate *in vitro* biomedical systems.

- The results confirm that the mass transfer rate depends significantly on the driving force and on the affinity between the substance and hydrogel. The substance flux increases as the initial concentration of the substance in a "stent" grows. The other examined process parameters (e.g. volumetric flow rate and liquid viscosity) did not significantly affect the process in the investigated range.
- The effective diffusion coefficient was calculated as a process parameter by fitting method for the basic experiment, and then used in the calculations for the other variants.
- Diffusion in hydrogel is the mechanism limiting mass transfer in the investigated system. For the first time, the diffusive model used in the literature, was applied to evaluate the theoretical mass of the substance released from a "stent". The provided calculations are consistent with the experimental data and therefore show that the model, despite its simplifications, allows to estimate the amount of released substance.
- The hypothetical situation proposing convection as the slowest stage of the process shows nonsensical results, supporting the claim that diffusion is limiting mass transfer.
- The prospect of determining the relative mass of the substance appearing in the subsequent parts of the system over time provides the opportunity to adjust the respective process parameters and therefore control the rate of mass transfer.
- The further work will focus on formulating the mathematical model, which will consist of a more precise description of the examined problem will be accompanied by the numerical modeling of the system and will provide a complex experimental verification. This will allow to analyze the active substance release from simulated biomedical systems more comprehensively.

SYMBOLS

c_{NC}	percentage concentration of New Coccine in solution, %
c_S	percentage concentration of substance in solution, %
$C_{0\,NC}$	initial percentage concentration of New Coccine in inner hydrogel, %
$C_{0\,RB}$	initial percentage concentration of Rhodamine B in inner hydrogel, %
$C_{0\,D}$	initial percentage concentration of Dopamine in inner hydrogel, %
$C_{0\,S}$	initial percentage concentration of substance in inner hydrogel, %
$C_{0\,PS}$	initial percentage concentration of Protein standard in inner hydrogel, %
C_S	molar concentration of substance in hydrogel, mol/ m^3
C_{S0}	molar initial concentration of substance in hydrogel, mol/ m^3
ΔC	mean driving force of mass transfer in liquid, mol/m^3
d	diameter of the coaxial aperture, where the solution ("blood") flows, m
D	diffusion coefficient of substance in liquid, m^2/s
$D_{S,H}$	diffusion coefficient of substance in hydrogel, m^2/s
$D_{NC,H}$	diffusion coefficient of New Coccine in hydrogel, m^2/s
F	surface of mass exchange; in this system the side surface of the coaxial aperture cylinder where the liquid flows, m^2
$f(t)$	relative mass of substance released from inner hydrogel at any given instance of time, defined by Equations (1) and (2), –
h	height of the coaxial aperture, where the solution ("blood") flows, m
k_L	convective mass transfer coefficient of substance in liquid, m/s
L	thickness of the inner hydrogel ("stent"), m
$m_S(t)$	mass of substance released from inner hydrogel ("stent") at a given instance of time, g
M_S	molar mass of the substance, kg/mol
m_{S0}	total mass of substance in a system, equal to the initial mass of substance in inner hydrogel ("stent") at $t = 0$, g
$m_{S\_Artery}(t)$	mass of substance in the outer hydrogel ("artery wall") at a given instance of time, g
$m_{S\_Blood}(t)$	mass of the substance in solution ("blood") at a given instance of time, g
$m_{S\_Stent}(t)$	mass of the substance in the inner hydrogel ("stent") at a given instance of time, g
$\Delta m_{S\,CONV}$	the mass of substance that could be drifted away by convection in the hypothetical situation where convection is the slowest stage of the process, g
$\Delta m_{S\,EXP}$	the mass of substance in liquid, determined experimentally, g
n	number of terms in the series, –
N'_A	mass flux of substance, mol/s
Q	volumetric flow of solution ("Blood"), ml/min
Pe	Peclet number, –
Re	Reynolds number, –
Sc	Schmidt number, –
Sh	Sherwood number, –
t	time, min or s
v	velocity, m/s

Greek symbols

μ	viscosity of liquid ("blood"), Pa·s
ρ	density of liquid ("blood"), kg/m^3

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