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EFFECTS OF DIFFERENT DRUG BINDING IN STENTED POROUS ARTERY TISSUE WALL: A NUMERICAL MODEL STUDY

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Abstract The emergence of drug-eluting stents has proved to be the most efficient methods in treating restenosis following percutaneous coronary intervention. This article deals with effects of specific as well as non-specific drug binding in the homogeneous permeable coronary vessel wall which follows the biodegradable polymer-based medicate conveyance from drug-eluting stents (DES). A three stage is considered, specifically, drug concentration in free phase, drug binding in extracellular matrix phase, and specific receptor phase, non-linear second order saturable reversible binding model. The most reason of the display work is appraisal of the degree of plausibility of modeling of specified non-specific binding within a homogeneous one-layered porous artery wall. A development in axis of symmetry drug delivery model has been noticed. The main focus in this present study consists of the influence of the Peclet number (Pe_T), Damköhler numbers (Da_1 and Da_2) and time dependent discharge kinetics. The outcome of this present work is of increase in tortuosity the diffusivity of drug increases. The present observation also demonstrates the binding in extracellular matrix phase is very low and high enough to specific receptor phase. Hence, the specific and non-specific binding plays a imperative part in the clinical adequacy of conveyed drugs locally, and it must be brought into thought within the levelheaded plan of stent-based conveyance frameworks.

1 Introduction

A drastic reduction has been noticed in the role of in-stent restenosis (a section of blocked artery that was opened up with angioplasty or a stent has become narrowed again) as a result of drug-eluting stents (DES), which releases anti-proliferative drugs into the arterial wall in a restricted manner. It has too revolutionized the treatment of coronary artery disease (CAD) to revive the deterred vessel that has become contracted since of atherosclerosis (a disease of the arteries characterized by the deposition of fats, cholesterol and other substances in and on the inner artery walls). Due to delayed healing of the wound infected during DES implantation, late stent thrombosis remains a safety concern of DES. The bare metal stents (BMS^s) which is active at the time, remains to be inadmissible as it is unable to anticipate in-stent restenosis (ISR). DES is a wire scaffold coated with therapeutic drug. Several DES are now implanted world-wide and various investigations are developed to discuss about its longevity and safety [1]. Now our aim is to describe the mechanism of drug uptake and it's binding within the arterial tissue.

In arrange to control the discharge rate of drug concentration, the coating may incorporate a rate-limiting impediment. To guarantee viable persuance of DES, the geometry of stent as well as coating design needs to be advanced such that restorative levels of drug are conveyed to the artery for the desired period of time [1]. When the drug is distributed in arterial tissue, the receptors bind the drug. Since, the bound drug becomes pharmacokinetically inactive, so it cannot produce its toxic effect and there are two types of binding, one is specific binding due to the specific receptor (SR) and the others is non-specific binding due to the extracellular matrix (ECM). The amount of drug eluted from the stent decides the success of anti-proliferative therapy from DES. Though, in most of the patients drug-eluting stents are the main alternative of percutaneous coronary interventions (PCI^s), its longevity and safety factors are still questionable.

As per study by Migliavacca et al. [18] the medicate discharge design in vascular fence from DES employing a single species access along with a partition coefficient approach to relate the free and bound medicate concentrations. The degeneration of polylactide acid (PLA) stent is seen as a result of series of non-linear binding into lactic acid and oligomers according to Ferreira et al. [7].

A number of different modeling approaches are available but only a few are considered as a nonlinear binding model [5]. Free and bound phases of drug in the tissue are included in this model. There is phenomenon of non-specific binding generated by association of drug with membrane components as well as to binding to specific receptor (SR). This is also generated by trapping of drug in the extracellular medium. Two equations for drug binding in vessel tissue are included by Tzafriri et al. [23] and McGinty et al. [17], one for specific binding to receptors and the other for non-specific binding to general extracellular matrix (ECM) sites. Thus, the results in three phases in the tissue are free and two bound (SR and ECM).

The present study discusses the freshness of the work as it includes two-species, setup of specific and non-specific binding in the arterial wall at distinctive stages which follows the medicate transportation eluted from stent struts where convection-diffusion-reaction process controls the transportation of free drug and reaction process governs the bound drugs (SR and ECM). On the surface of the struts [16] a time dependent delivery is appointed. Within the arterial tissue the porosity and the tortuosity of the arterial wall control the drug transport. The present study deals with a complete understanding of the role of specific and non-specific drug binding in arterial drug distribution, stent design, drug composition, release formulation and the significance of porosity and tortuosity on the diffusion of medicate can be better optimized.

2 Geometrical description

The computational region consists of an portion towards axial direction of measurement L and the wall breadth is 10 times the strut dimension (δ). Three stent struts have been considered in this study with interstrut distances 6 times the strut measurement (δ) [cf. Fig. 1] [16]. The concentration of free medicate is indicated by c_f, the concentration of bound medicate bound to non-specific general extracellular phase in the vessel, is alluded to as ECM-bound medicate which is indicated by $c_{b_{ECM}}$ and the concentration of bound drug which is bound to specific receptors is alluded to as SR-bound drug which is indicated by $c_{b_{SR}}$ respectively.

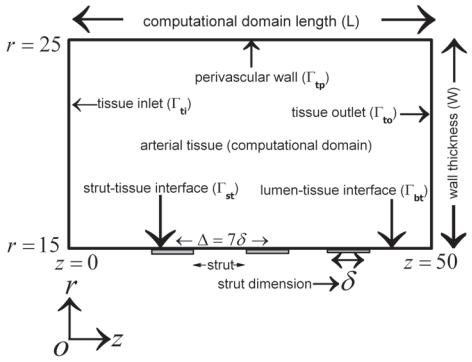

Figure 1. Diagramatic representation of computational model in this study.

3 Drug transport and binding formulation

There are different binding formulations described by the following dimensional manner [3, 11]:

$$\frac{\partial \bar{c}_f}{\partial \bar{t}} + \frac{\gamma_w}{\varepsilon_w}\frac{\partial (V_{wall}\bar{c}_f)}{\partial \bar{r}} = D_T\left[\frac{\partial^2 \bar{c}_f}{\partial \bar{r}^2} + \frac{1}{\bar{r}}\frac{\partial \bar{c}_f}{\partial \bar{r}} + \frac{\partial^2 \bar{c}_f}{\partial \bar{z}^2}\right] - \frac{\partial \bar{c}_{b_{ECM}}}{\partial \bar{t}} - \frac{\partial \bar{c}_{b_{SR}}}{\partial \bar{t}}, \tag{3.1}$$

$$\frac{\partial \bar{c}_{b_{ECM}}}{\partial \bar{t}} = \left[k_{on}^{ECM}\bar{c}_f\left(\bar{c}_{b_{ECM}}^{max} - \bar{c}_{b_{ECM}}\right) - k_{on}^{ECM}K_d^{ECM}\bar{c}_{b_{ECM}}\right], \tag{3.2}$$

$$\frac{\partial \bar{c}_{b_{SR}}}{\partial \bar{t}} = \left[k_{on}^{SR}\bar{c}_f\left(\bar{c}_{b_{SR}}^{max} - \bar{c}_{b_{SR}}\right) - k_{on}^{SR}K_d^{SR}\bar{c}_{b_{SR}}\right], \tag{3.3}$$

where, D_T , the true drug diffusivity may be written as the following way [12, 20]

$$D_T = [1 + \frac{B_M}{K_d}] \times D_{eff}, \tag{3.4}$$

here

$$D_{eff} = \frac{\varepsilon_w}{\tau_w} \times D_{free}. \tag{3.5}$$

Here, both ε_w , the porosity and τ_w , the tortuosity of the arterial vessel; D_{free}, the coefficient of free diffusivity and D_{eff}, the coefficient of effective diffusivity; B_M, the total binding capacity and K_d, the association rate.

At the proximal (Γ_{ti}) and the distal (Γ_{to}) arterial walls, a boundary condition applied as [9] follows

$$\frac{\partial \bar{c}_f}{\partial \bar{z}} = 0 = \frac{\partial \bar{c}_{b_{ECM}}}{\partial \bar{z}} = \frac{\partial \bar{c}_{b_{SR}}}{\partial \bar{z}} \text{ on } \Gamma_{ti} \text{ and } \Gamma_{to}, \tag{3.6}$$

At perivascular wall (Γ_{tp}), tissue-lumen (Γ_{bt}) interface and tissue-strut (Γ_{st}) interface, impermeable boundary condition for both bound drugs are applied as

$$\frac{\partial \bar{c}_{b_{ECM}}}{\partial \bar{r}} = 0 = \frac{\partial \bar{c}_{b_{SR}}}{\partial \bar{r}} \text{ on } \Gamma_{tl} \ (= \Gamma_{bt} \cup \Gamma_{st}) \text{ and } \Gamma_{tp}, \tag{3.7}$$

The condition for free drug ($\bar{c}_f$) [5] is applied as

$$\bar{c}_f = 0 \text{ on } \Gamma_{tp}, \tag{3.8}$$

At lumen-tissue interface (Γ_{bt}), zero-concentration or zero-flux boundary condition is applied as [13]

$$\bar{c}_f = 0 \text{ or } \frac{\partial \bar{c}_f}{\partial \bar{r}} = 0 \text{ on } \Gamma_{bt}, \tag{3.9}$$

Drug elution from drug eluting stent is modeled as [8, 19]

$$\bar{c}_f = c_s \exp\left(-\bar{\lambda}\bar{t}\right) ; \bar{t} \geq 0 \text{ on } \Gamma_{st}, \tag{3.10}$$

where c_s is the starting amount of medicate on the stent; $\bar{\lambda}$, discharge rate of stent.

To obtain well-behaved computations, the parameters and the variables are making dimensionless as follows:

$$x = \frac{\bar{r}}{\delta}, \quad z = \frac{\bar{z}}{\delta}, \quad t = \frac{\bar{t}.V_{wall}}{\delta},$$
$$c_f = \frac{\bar{c}_f}{c_s}, \quad c_{b_{ECM}} = \frac{\bar{c}_{b_{ECM}}}{c_{b_{ECM}}^{max}}, \quad c_{b_{SR}} = \frac{\bar{c}_{b_{SR}}}{c_{b_{SR}}^{max}}$$

Under these assumptions, the above equations (eqs. 3.1–3.10) becomes the dimensionless forms as follows:

$$\begin{aligned}
\frac{\partial c_f}{\partial t} + \frac{\gamma_w}{\varepsilon_w}\frac{\partial c_f}{\partial r} &= \frac{1}{Pe_T}\left[\frac{\partial^2 c_f}{\partial r^2} + \frac{1}{r}\frac{\partial c_f}{\partial r} + \frac{\partial^2 c_f}{\partial z^2}\right] \\
&\quad -\frac{1}{\alpha}\frac{\partial c_{b_{ECM}}}{\partial t} - \frac{1}{\beta}\frac{\partial c_{b_{SR}}}{\partial t}, && (3.11)\\
\frac{\partial c_{b_{ECM}}}{\partial t} &= \frac{\alpha.Da_1}{Pe_1}\left[c_f(1 - c_{b_{ECM}}) - \alpha_1 c_{b_{ECM}}\right], && (3.12)\\
\frac{\partial c_{b_{SR}}}{\partial t} &= \frac{\beta.Da_2}{Pe_2}\left[c_f(1 - c_{b_{SR}}) - \beta_1 c_{b_{SR}}\right], && (3.13)\\
\frac{\partial c_f}{\partial z} &= 0 = \frac{\partial c_{b_{ECM}}}{\partial z} = \frac{\partial c_{b_{SR}}}{\partial z} \text{ on } \Gamma_{ti} \text{ and } \Gamma_{to}, && (3.14)\\
\frac{\partial c_{b_{ECM}}}{\partial r} &= 0 = \frac{\partial c_{b_{SR}}}{\partial r} \text{ on } \Gamma_{tl} \ (= \Gamma_{bt} \cup \Gamma_{st}) \text{ and } \Gamma_{tp}, && (3.15)\\
c_f &= 0 \text{ on } \Gamma_{tp}, && (3.16)\\
c_f &= 0 \text{ or } \frac{\partial c_f}{\partial r} = 0 \text{ on } \Gamma_{bt}, && (3.17)\\
c_f &= \exp(-\lambda t)\ ; t \geq 0 \text{ on } \Gamma_{st}, && (3.18)
\end{aligned}$$

where the Peclet numbers (Pe_T, Pe_1 and Pe_2), the Damköhler numbers (Da_1 and Da_2), equilibrium dissociation constants (K_d^{ECM} and K_d^{SR}), the setting parameters (α, α_1, β and β_1) and dimensionless rate constant (λ) are as:

$$Pe_T = \frac{V_{wall}.\delta}{D_T}, \quad Pe_1 = \frac{V_{wall}.\delta}{D_T^{ECM}}, \quad Pe_2 = \frac{V_{wall}.\delta}{D_T^{SR}},$$
$$Da_1 = \frac{k_{on}^{ECM}.c_{b_{ECM}}^{max}.\delta^2}{D_T^{ECM}}, \quad Da_2 = \frac{k_{on}^{SR}.c_{b_{SR}}^{max}.\delta^2}{D_T^{SR}},$$
$$K_d^{ECM} = \frac{k_r^{ECM}}{k_{on}^{ECM}}, \quad K_d^{SR} = \frac{k_r^{SR}}{k_{on}^{SR}}, \quad \alpha = \frac{c_s}{c_{b_{ECM}}^{max}},$$
$$\alpha_1 = \frac{K_d^{ECM}}{c_s}, \quad \beta = \frac{c_s}{c_{b_{SR}}^{max}}, \quad \beta_1 = \frac{K_d^{SR}}{c_s}, \quad \lambda = \frac{\lambda.\delta}{V_{wall}},$$

where k_r^{ECM} and k_r^{SR} are respectively the dissociation rate constant of ECM drug binding and SR binding site in the arterial tissue.

Here, D_T^{ECM} and D_T^{SR} are, respectively, the true diffusivities of the ECM-bound drug and the SR-bound drug can be defined as:

$$D_T^{ECM} = [1 + \frac{c_{b_{ECM}}^{max}}{K_d^{ECM}}] \times D_{eff},$$
$$D_T^{SR} = [1 + \frac{c_{b_{SR}}^{max}}{K_d^{SR}}] \times D_{eff},$$

where the effective diffusivity (D_{eff}) of the free drug.

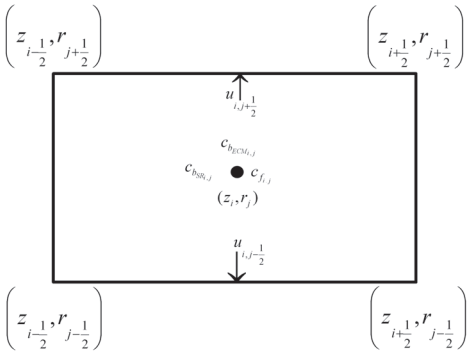

Figure 2. Representation of MAC cell for tissue.

4 Solution procedure

The resulting systems of non-dimensionalized partial differential equations (PDE^s) are then spatially discretized by using a standard finite difference scheme. In this sort of mesh arrangement, the drug of free-phase, ECM-phase and SR-phase bound at the centre of the cells [cf. Fig. 2] were calculated. The time derivative terms is discretized on the basis of first order accurate two-level time-differencing formulae. A hybrid formulae containing of central differencing with second order upwinding is applied for the convection. However, the diffusive terms in the equations have been discretized using second order three-point (accurate) central difference formulae. For details of the numerical procedure, readers may follow to Saha et al. [21].

5 Outcomes and analysis

In Table 1, I summarise the parameter values used in the simulations. Solutions are estimated with mesh sizes 50×101 for $\delta t = 0.0001$ [6, 17].

Figure 3a-c respectively shows the behaviour of the concentration of free-phase, ECM-phase bound and SR-phase bound medicate for three distinct times. It is clear from above pictures that with rising of time, free, ECM-bound and SR-bound masses falling-off. The rate of falling-off of the free phase is quicker than the ECM-phase bound although the SR-phase bound is slower than the ECM-phase bound. As a result, drug enters the vessel wall within the free part and rapidly bound to ECM- and SR- binding sections. The drug concentration of free and ECM bound section profiles reach to top level (display in Figure 3d) before decaying with the time since drug traverses through the vessel, is bound to specific receptor binding section and absorbed at the adventitial boundary($r = 25$). Though the free and ECM-bound part profile pictures are same, concentration of drug in the SR-bound part are bigger than the ECM-bound part that successively higher than the concentrations of free drug. SR-bound drug concentrations spanning thirty percent of the thickness of the vessel is saturated within the time $t = 10$: these stay saturated for the length of time $t = 200$ as observed (Figure 3c). The remaining specific receptor sites become saturated within the subsequent times and they too remain at saturation levels for the period of time $t = 300$. In figure 3d, the temporal variation of normalized average concentration of drug profiles indicates that the SR-bound section drug binding is higher than the ECM-bound section binding drug. Thus, the results based on the calculation as per the observations show that drug conveyed to the arterial vessel wall from the stent is too low to occupy a large proportion of ECM binding sections, nevertheless is high enough to saturate specific receptor binding sections that agrees with Tzafriri et al. [23].

Figure 4a-c respectively show the time-dependent concentration sketches for free-phase, ECM-phase bound and SR-phase bound concentrations within the tissue for distinct positions towards radial direction. A decrease in the medicate masses (free-phase, ECM-phase bound and SR-phase bound) has been observed with the increasing radial positions (from lumen-tissue in-

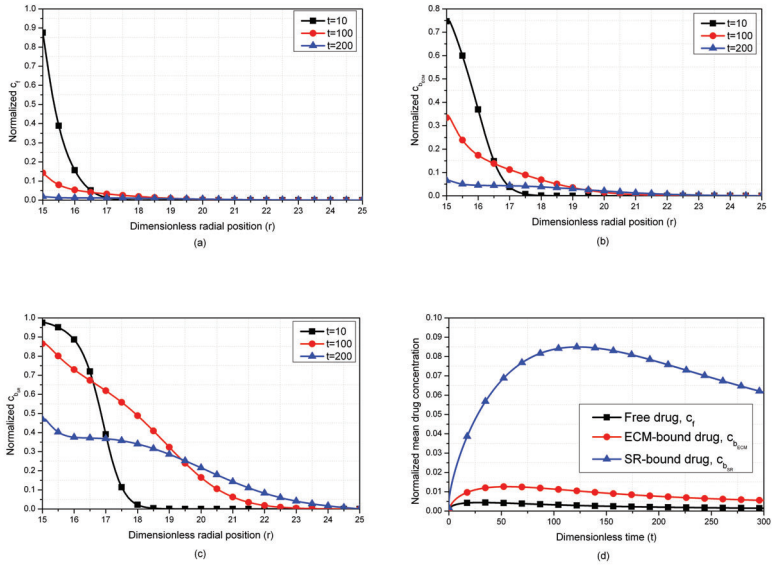

Figure 3. Variation of concentration of drug within the artery wall with radial positions for various times. **(a)** c_f, **(b)** c_{ECM}, **(c)** c_{SR}. **(d)** dimensionless drug mass in every phase.

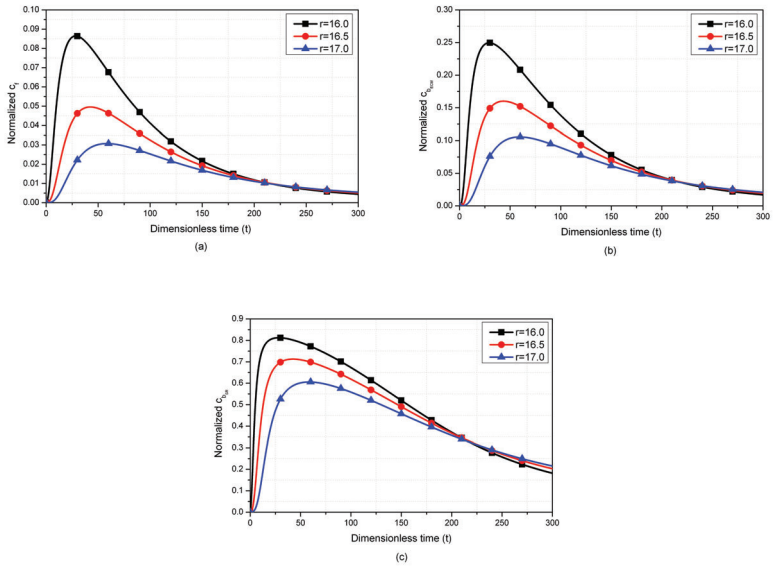

Figure 4. Variation of concentration of drug within the artery wall with time for various radial positions. **(a)** c_f, **(b)** c_{ECM}, **(c)** c_{SR}.

terface). However the characteristic of the graphs, some areas are found to be quite similar as predicted, binding and unbinding processes take place at the same time. The concentration of drug at the interface remains to be at its supreme value for all time. It is good agreement of McGinty et al. [17].

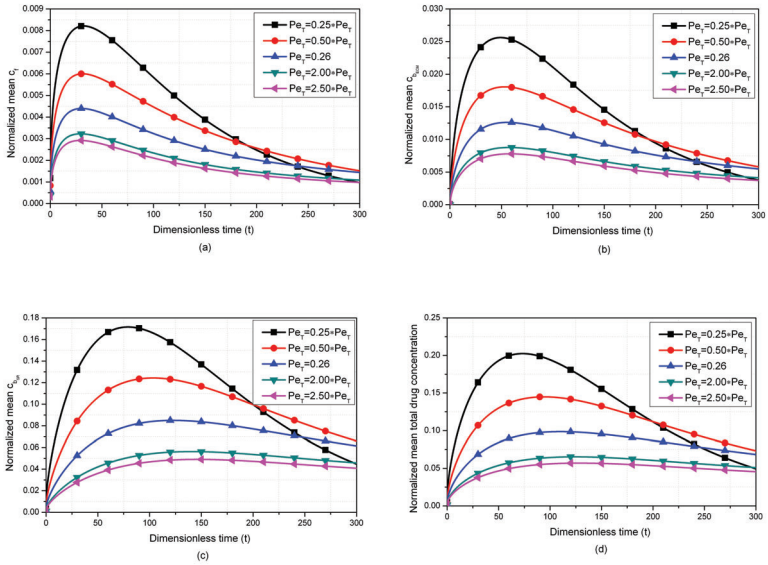

Figure 5. Variation of concentration of mean drug within the artery wall with time for various Peclet numbers Pe_T. **(a)** c_f, **(b)** c_{ECM}, **(c)** c_{SR}, **(d)** bulk drug.

Figure 5a-d respectively shows the circulations of standardised average free-phase drug, average ECM-phase bound drug, average SR-phase bound drug and average bulk drug concentrations over the entire period of time for distinct values of Peclet number Pe_T. It is realized, in each case first an increase in the drug mass up to some upper bound is observed and then there is a decrease asymptotically. Evidently, Pe_T, depends on D_T, again D_T depends on D_{eff}, which further rises with a falling-off of the porosity (ε_w) and also with an rise of the tortuosity (τ_w). Based on the observations from the figures it is found that there is a decrease in the average medicate (free-phase, ECM-phase bound, SR-phase bound and bulk) concentrations with falling-off porosity and rising tortuosity of the artery wall (i.e. rising of Peclet number (Pe_T)).

Over the entire period of time (Figure 6a-d) the effect of α is exhibited on the normalized average free, average SR-bound, average SR-bound and average bulk drug concentrations. The results shown in the figures are an evidence that, there is an increase α (depending on $c_{b_{ECM}}^{max}$) with a falling-off of the ECM-phase binding site density ($c_{b_{ECM}}^{max}$) (taking c_s is unchanged). Our observation persist that all the average medicate (free-phase, ECM-phase bound, SR-phase bound and bulk) concentrations rise if the ECM binding site density falling-off.

The impact of setting parameter β on the standardised average free-phase, average ECM-phase bound, average SR-phase bound and average bulk concentration of drug interior the vessel tissue over the entire period of time is displayed in Figure 7a-d, severally. There is also an increase β (depending on $c_{b_{SR}}^{max}$), with a falling-off the receptor binding phase density ($c_{b_{SR}}^{max}$) (taking c_s is unchanged). Naturally the average free-phase, ECM-phase bound, SR-phase bound and bulk concentrations increases if the receptor binding site density decreases.

Finally, the spatial distribution of free-phase, ECM-phase bound and SR-phase bound drug concentration is displayed in Figure 8a-c, respectively, which again justifies the minimization of late lumen drop at the distant portion of the vessel, thus the observations of Balakrishnan et al. [2] is validated consequently.

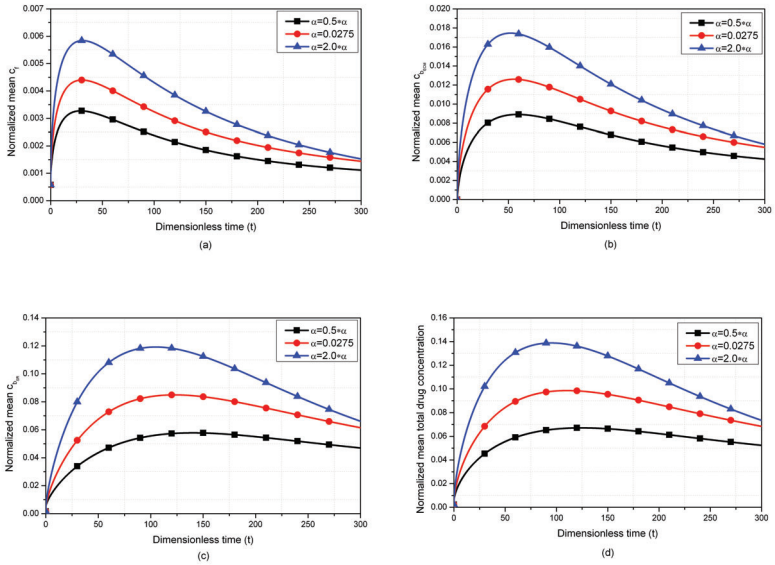

Figure 6. Alteration of concentration of mean drug within the artery wall with time for various values of α. **(a)** c_f, **(b)** c_{ECM}, **(c)** c_{SR}, **(d)** bulk drug.

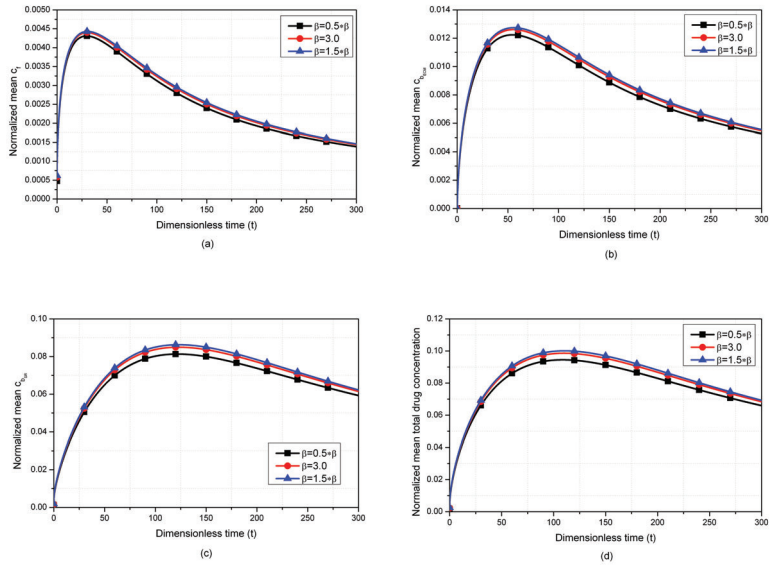

Figure 7. Variation of concentration of mean drug within the artery wall with time for different β. **(a)** c_f, **(b)** c_{ECM}, **(c)** c_{SR}, **(d)** bulk drug.

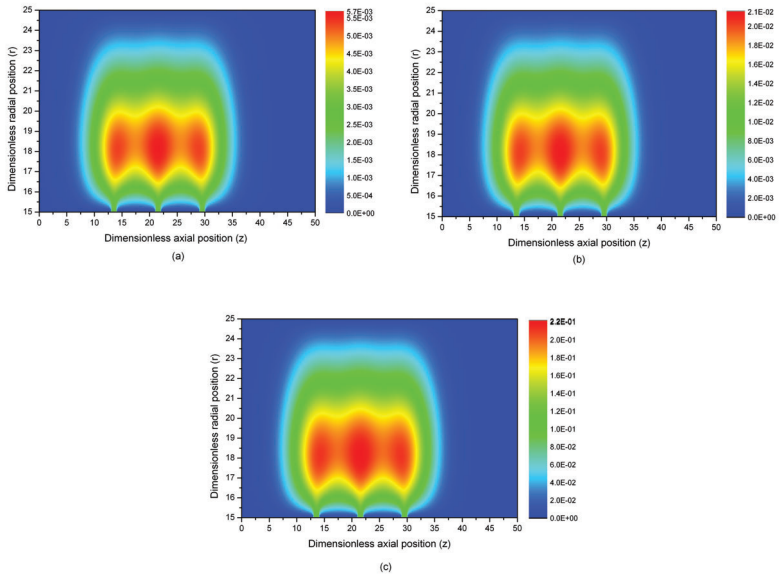

Figure 8. Ocular image representation of concentration of drug within artery for time-variant discharge kinetics with no concentration gradient intermix situation at blood-tissue interface Γ_{bt}. **(a)** c_f, **(b)** c_{ECM}, **(c)** c_{SR}.

Table 1. Credible values of concerned parameters

Parameters	Numerical values	Sources	Parameters	Numerical values	Sources
δ	10^{-4} m	[2]	$\bar{\lambda}$	10^{-5} s^{-1}	[15]
c_s	10^{-2} mol m^{-3}	[2]	λ	0.02	[Our study]
V_{wall}	5.8×10^{-8} m s^{-1}	[10]	ε_w	0.787	[20]
$c_{b_{ECM}}^{max}$	3.63×10^{-1} mol m^{-3}	[22]	γ_w	1	[6]
$c_{b_{SR}}^{max}$	3.3×10^{-3} mol m^{-3}	[23]	τ_w	1.333	[20]
B_M	1.3 mol m^{-3}	[12]	Pe_T	0.26	[Our study]
k_{on}^{ECM}	2.0 [mol m^{-3} s]$^{-1}$	[22]	Pe_1	0.02	[Our study]
k_{on}^{SR}	8.0×10^2 [mol m^{-3} s]$^{-1}$	[22]	Pe_2	0.15	[Our study]
K_d	0.136 mol m^{-3}	[12]	Da_1	24	[Our study]
K_d^{ECM}	2.6×10^{-3} mol m^{-3}	[22]	Da_2	700	[Our study]
K_d^{SR}	2.0×10^{-4} mol m^{-3}	[22]	α	0.0275	[Our study]
k_r^{ECM}	5.2×10^{-3} s^{-1}	[23]	α_1	0.26	[Our study]
k_r^{SR}	1.6×10^{-4} s^{-1}	[23]	β	3.0	[Our study]
D_{free}	3.65×10^{-12} m^2 s^{-1}	[22]	β_1	0.02	[Our study]

6 Conclusion and forthcoming research area

A two-dimensional axis of symmetry model has been used and the drug distribution is governed by convection-diffusion-reaction equation, whereas the retention of drug by a non-linear reversible chemical reaction only. The main goal of this work is to investigate the eluted drug from strut surfaces moves randomly around the arterial tissue and interact with the receptors presence in cell membrane. The receptors bind the drug molecules in binding site and there are another site of binding which is non-specific binding and the bulk drug binding within the vessel wall is the sum of specific and non-specific drug binding.

The conclusions of the above investigations are the following:

• The free-phase, ECM-phase bound and SR-phase bound drug masses decreases with rising time.

• The rate of falling-off the free-phase drug is quicker than the ECM-phase bound drug while the specific receptor-phase bound drug is slower than the ECM-phase bound drug.

• The concentration of drug at the interface remains to be at its maximum value for all time.

• The average free-phase, ECM-phase bound, SR-phase bound and bulk drug falling-off with falling-off porosity and rising tortuosity of the vessel wall.

• The average free-phase, ECM-phase bound, SR-phase bound and bulk drug rise if the extracellur matrix binding site density decreases.

• The average free-phase , ECM-phase bound, SR-phase bound and bulk drug rises if the receptor binding site density decreases.

As a matter of fact, vascular wall is a constitution of various layers with various diffusivity property, therefore consideration of different layers needs to be addressed. Also for simplicity a number of assumptions are taken in the present model, namely the influence of stent coating and luminal flow which are ignored [3, 4, 17].

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References

[1] J. Aragon, S. Kar, F. Tio, B. Trauthen, A. Parisky, C. Watanabe, A. Jamali, N. Eigler, P. W. Serruys and F. Litvack, The effect of variable release kinetics on paclitaxel efficacy from a drug eluting stent in a porcine model, *EuroIntervention : Journal of Euro PCR in collaboration with the Working Group on Interventional Cardiology of the European Society of Cardiology* **1(2)**, 228–235 (2005).

[2] B. Balakrishnan, A. R. Tzafriri, P. Seifert, A. Groothuis, C. Rogers and E. R. Edelman, Strut position, blood flow, and drug deposition implications for single and overlapping drug-eluting stents, *Circulation*, **111(22)**, 2958-2965 (2005).

[3] B. Balakrishnan, J. F. Dooley, G. Kopia and E. R. Edelman, Intravascular drug release kinetics dictate arterial drug deposition, retention, and distribution, *Journal of Controlled Release*, **123(2)**,100-108 (2007).

[4] A. Borghi, E. Foa, R. Balossino, F. Migliavacca and G. Dubini, Modelling drug elution from stents: effects of reversible binding in the vascular wall and degradable polymeric matrix, *Computer Methods in Biomechanics and Biomedical Engineering*, **11(4)**, 367-377 (2008).

[5] F. Bozsak, J. M. Chomaz and A. I. Barakat, Modeling the transport of drugs eluted from stents: physical phenomena driving drug distribution in the arterial wall, *Biomechanics and Modeling in Mechanobiology*, **13(2)**, 327-347 (2014).

[6] J. Ferdous and C. Chong, Effect of atherosclerotic plaque on drug delivery from drug-eluting stent, *In: 13th International Conference on Biomedical Engineering, Springer*, **pp**, 1519-1522 (2009).

[7] J. Ferreira, J. Naghipoor and P. de Oliveira, A coupled non-fickian model of a cardiovascular drug delivery system, *Mathematical Medicine and Biology: a journal of the IMA*, **33(3)**, 329-357 (2016).

[8] T. Higuchi, Mechanism of sustained-action medication. theoretical analysis of rate of release of solid drugs dispersed in solid matrices, *Journal of Pharmaceutical Sciences*, **52(12)**, 1145-1149 (1963).

[9] M. Horner, S. Joshi, V. Dhruva, S. Sett and S. Stewart, A two-species drug delivery model is required to predict deposition from drug-eluting stents, *Cardiovascular Engineering and Technology*, **1(3)**, 225-234 (2010).

[10] Z. Huang and J. Tarbell, Numerical simulation of mass transfer in porous media of blood vessel walls, *The American journal of Physiology*, **273(1)**, H464-H477 (1997).

[11] C. W. Hwang, D. Wu and E. R. Edelman, Physiological transport forces govern drug distribution for stent-based delivery, *Circulation*, **104(5)**,600-605 (2001).

[12] V. B. Kolachalama, S. D. Pacetti, J. W. Franses, J. J. Stankus, H. Q. Zhao, T. Shazly, A. Nikanorov, L. B. Schwartz, A. R. Tzafriri and E. R. Edelman, Mechanisms of tissue uptake and retention in zotarolimus-coated balloon therapy, *Circulation*, **127(20)**, 2047-2055 (2013).

[13] K. Kolandaivelu, C. C. O'Brien, T. Shazly, E. R. Edelman and V. B. Kolachalama, Enhancing physiologic simulations using supervised learning on coarse mesh solutions, *Journal of The Royal Society Interface*, **12(104)**, 20141073 (2015).

[14] A. D. Levin, N. Vukmirovic, C. W. Hwang and E. R. Edelman, Specific binding to intracellular proteins determines arterial transport properties for rapamycin and paclitaxel, *Proceedings of the National Academy of Sciences of the United States of America*, **101(25)**, 9463-9467 (2004).

[15] S. McGinty, S. McKee, R. M. Wadsworth and C. McCormick, Modelling drug-eluting stents, *Mathematical Medicine and Biology*, **28(1)**, 1-29 (2011).

[16] S. McGinty and G. Pontrelli, A general model of coupled drug release and tissue absorption for drug delivery devices, *Journal of Controlled Release*, **217**,327-336 (2015).

[17] S. McGinty and G. Pontrelli, On the role of specific drug binding in modelling arterial eluting stents, *Journal of Mathematical Chemistry*, **54(4)**, 967-976 (2016).

[18] F. Migliavacca, F. Gervaso, M. Prosi, P. Zunino, S. Minisini, L. Formaggia and G. Dubini, Expansion and drug elution model of a coronary stent, *Computer Methods in Biomechanics and Biomedical Engineering*, **10(1)**, 63-73 (2007).

[19] C. C. O'Brien, V. B. Kolachalama, T. J. Barber, A. Simmons and E. R. Edelman, Impact of flow pulsatility on arterial drug distribution in stent-based therapy, *Journal of Controlled Release*, **168(2)**, 115-124 (2013).

[20] B. M. O'Connell and M. T. Walsh, Demonstrating the influence of compression on artery wall mass transport, *Annals of Biomedical Engineering*, **38(4)**,1354-1366 (2010).

[21] R. Saha and P. K. Mandal, Modelling Time-dependent Release Kinetics in Stent-based Delivery, *Journal of Exploratory Research in Pharmacology*, **3**, 61-70 (2018).

[22] A. R. Tzafriri, A. D. Levin and E. R. Edelman, Diffusion-limited binding explains binary dose response for local arterial and tumour drug delivery, *Cell Proliferation*, **42(3)**, 348-363 (2009).

[23] A. R. Tzafriri, A. Groothuis, G. S. Price and E. R. Edelman, Stent elution rate determines drug deposition and receptor-mediated effects, *Journal of controlled release*, **161(3)**, 918-926 (2012).

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