



Research Article

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# Modelling of Drug Release from a Polymer Matrix System



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## Abstract

A drug release model is proposed to predict the behaviour of an oral drug tablet as it traverses the gastrointestinal (GI) tract. The model predicts the rate of change of tablet dimensions. The effect of polymer degradation rate on the tablet dissolution time and drug release kinetics is analyzed. The total tablet dissolution time decreases with increase in the polymer degradation rate constant ( $k_d$ ). A simpler second model (power law) is also offered to describe the relationship between tablet dissolution time and  $k_d$ . The model predicts initial burst release of the drug followed by nearly constant release. The time of burst release and the amount of drug undergoing burst release decreases with increases in the  $k_d$ .

**Keywords:** Drug release model; Drug diffusion; Polymer matrix swelling; Polymer dissolution; Release kinetics

**Abbreviations:** HPMC: Hydroxy Propyl Methyl Cellulose; PEO: Polyethylene Oxide; PDE's: Partial Differential Equations; ODE's : Ordinary Differential Equations

## Introduction

There has been a significant change in the performance of drug delivery systems in the last 100 years. The delivery systems have evolved from simple pills to sustained controlled release and sophisticated programmable delivery systems [1]. Uncontrolled and immediate drug release kinetics is the characteristic of traditional delivery systems. This mainly led to abrupt increase in drug concentration on body tissues crossing the toxic threshold and then falling off below the minimum effective therapeutic level. The development of controlled drug delivery systems has greatly helped in addressing this issue, and in maintaining the drug concentration in the blood and other tissues at a desired level for a longer time. In a controlled drug release system, a burst of drug is initially released to rapidly provide the drug effective therapeutic concentration; this is followed by controlled release to maintain the drug concentration at the desired level. The development of controlled release systems has greatly improved patient compliance and drug effectiveness; in addition there is a reduction in the frequency of dosage administration and less side effects. Thus the design and development of controlled release systems has become a key issue in current research. The use of computational modelling in this process has been very useful. For example modelling helps in predicting the drug

release kinetics from a controlled release system and helps in further improvement in the design and development process.

The most common strategy to obtain a controlled drug release is by embedding a drug in a polymer matrix. The polymer used for this purpose can be a hydrophobic or a hydrophilic matrix depending on the nature of the drug. Some of the hydrophobic polymers include wax, polyethylene, polypropylene and ethyl cellulose. Some of the hydrophilic polymers are hydroxy propylcellulose, hydroxy propylmethylcellulose, methylcellulose, sodium carboxymethylcellulose, alginates and scleroglucan [2]. The drug release mechanism from a polymer matrix can be categorized based on three different processes as follows:

- Drug diffusion from a non-biodegradable polymer (diffusion-controlled system)
- Drug diffusion from a swellable polymer (swelling-controlled system)
- Drug release due to polymer degradation and erosion (erosion-controlled system)

All the above-mentioned processes have a diffusion

component. For a non-biodegradable polymer matrix, drug release is due to the concentration gradient caused by diffusion or polymer swelling. For a biodegradable polymer matrix, release is either controlled by polymer chain disentanglement, which leads to matrix erosion, or by diffusion when the erosion process is slow [3,4]. There are several mathematical models proposed for drug release from tablets of different geometries as discussed above [5,6]. In this paper we describe a model first discussed by us in Pavurala & Achenie [7] but in greater detail here.

## Diffusion-controlled systems

Diffusion-controlled systems are generally modelled using Fick's law of diffusion with appropriate boundary conditions. For example, Eq. 1 gives the diffusion from a spherical micro particle.

$$\frac{\partial C}{\partial t} = \frac{1}{r^2} \frac{\partial}{\partial r} \left[ D r^2 \frac{\partial C}{\partial r} \right] \quad (1)$$

Where, the diffusion is assumed to be in the radial direction, D and C are the diffusion coefficient and the concentration of the drug in the polymer matrix. The boundary conditions are based on the mass transfer processes at the surface and the bulk surrounding the micro particle.

A reservoir system is a very good example of a diffusion-controlled system. In that system, the assumption is that the drug is confined in a spherical shell of inner radius ( $R_i$ ) and outer radius ( $R_o$ ) and the diffusion of drug takes place through the shell thickness of ( $R_o - R_i$ ). The Fick's law defined in Eq. 1 is solved, with boundary conditions defined as in Eq. 2,

$$\begin{aligned} r = R_i & \quad C = C_r \\ r = R_o & \quad C = 0 \end{aligned} \quad (2)$$

Where, the concentration of drug at the inner radius ( $R_i$ ) is kept at a constant reservoir drug concentration ( $C_r$ ) and the concentration at the outer radius ( $R_o$ ) is assumed to be zero, since the surrounding bulk volume is large and there is no other mass transfer limitation [8].

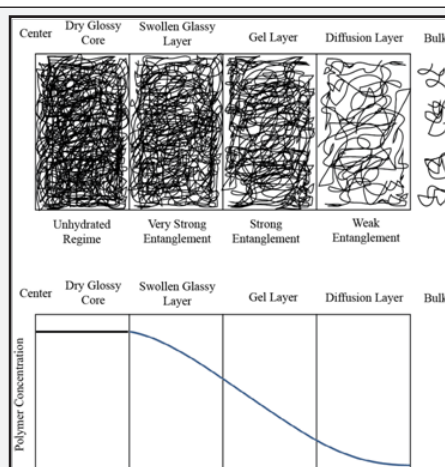
## Modeling - Literature Review

### Matrix systems

In a typical matrix system, the drug is uniformly distributed within a non-biodegradable polymer matrix. The mechanism of drug release from a matrix system is dependent on the initial drug loading of the tablet and the solubility of drug in the polymer matrix. When the initial drug loading is lower than the drug solubility, the drug is assumed to be uniformly distributed in the polymer matrix. These kinds of systems are known as dissolved drug systems. In contrast, in a dispersed drug system the initial drug loading is higher than the drug solubility inside the polymer system. Here the system is divided into two regions namely, the non-diffusing region, where the undissolved drug is at the initial drug loading concentration and the diffusion region where the diffusion of the dissolved drug takes place. The drug diffusion through the diffusion region leads to shrinking of the non-diffusing region. Thus the boundary between the non-diffusing and the diffusing region continuously moves making it a moving-boundary problem [8,9].

### Swelling-controlled release systems

Swelling-controlled systems generally consist of a uniformly distributed drug within a biodegradable, swellable polymer. These swellable polymers are hydrophilic in nature so that when in contact with water, the latter is absorbed into the polymer, thereby swelling the polymer matrix. The swelling helps in loosening the polymer entanglement leading to disentanglement of the polymer. The polymer matrix swelling leads to the formation of a rubbery region, where there is better drug mobility due to lower polymer concentration. This helps in enhancing the release characteristics of the drug that is not only dependent on the diffusion rate of the drug but also on the polymer disentanglement and dissolution processes. A schematic showing the effect of polymer concentration on the polymer disentanglement rate is shown in Figure 1.



**Figure 1:** Schematic of polymer matrix disentanglement level as a function of polymer concentration in a swelling-controlled release system (redrawn from Ju et al. 1995).

As the polymer absorbs water, there is a change in concentration of the polymer in the matrix. The polymer concentration is very high in the dry glassy core. The water diffusion in the swollen glassy layer creates a more mobile network, but restricted by very strong chain entanglement. In the gel layer, the concentrations of water and polymer become comparable with some reduction in the chain entanglement. Ultimately, the diffusion layer becomes very rich in water concentration, leading to weak chain entanglement and the polymer starts to disentangle and dissolve at the interface [6].

### Modeling of tablet swelling and dissolution

The modelling of drug release from polymer matrices can greatly improve the design and understanding of delivery systems. Availability of a reliable mathematical model could complement/augment the resource-consuming trial and-error procedures usually followed in the manufacture of drug delivery systems. Several modelling approaches are presented in the literature; those that are relevant to this work are described below.

Modeling drug release behaviour by swelling and dissolving in polymer matrices described in the literature considers either polymer slabs or spheres [10,11], very few models consider the cylindrical geometry of tablets [12-16]. Tablet models tend to employ simplified one-dimensional transport assumptions [17,18].

The model by [19] considered drug release from a swelling and dissolving cylindrical polymeric tablet and can predict drug release from formulations containing soluble as well as poorly soluble drugs. The mass transfer rate includes the contributions from diffusion as well as swelling (diffusion induced convection). The transformation from solid to gel phase is assumed to be limited by the rate of penetrant transport into the solid phase, corresponding to a critical penetrant concentration. At the gel-solvent interface, it is assumed that equilibrium exists between the hydrodynamic forces and polymer entanglement. This implies that the surface polymer concentration reaches a constant value after the initial phase and that this equilibrium exists for the rest of the dissolution process. Hence, the initial polymer dissolution rate is zero, until the entanglement strength has been reduced by the increased penetrant concentration. The model was used to study the influence of the drug diffusion coefficient, the drug solubility and the initial drug loading on the drug release profile. The model presented in this paper can simulate the drug and polymer release from swelling and dissolving polymer tablet. The model was verified against drug release and polymer dissolution data for the slightly soluble drug Methyl Paraben and the soluble drug Saligenin, showing good agreements in both cases. The drug diffusion coefficient was fitted to data, and the values obtained were considered to be accurate, thus confirming the reliability of the model Table 1.

**Table 1:** Effect of polymer degradation rate on the tablet dissolution time.

Polymer Degradation Rate Constant ( $k_d$ ) (Mm/Min)	Tablet Dissolution Time (Min)
0.012	231.2500
0.024	123.7500
0.036	85.6240
0.048	68.1250
0.06	47.5000
0.072	40.0000
0.084	34.3330
0.096	30.2500
0.108	27.0830
0.12	24.5000

The immersion of pure Hydroxy Propyl Methyl Cellulose (HPMC) tablets in water and their water uptake, swelling and the erosion during immersion were investigated in drug-free and drug-loaded systems [20]. A novel approach by image analysis to measure polymer and water masses during hydration was described. It was found that the model consisting of the transient mass balance, accounting for water diffusion, diffusivity change due to hydration, swelling and erosion, was able to reproduce experimental data.

In Kiil and Dam-Johansen [18], a detailed mathematical model capable of estimating radial front movements, transient drug fluxes, and cumulative fractional drug release behaviours from a high-viscosity HPMC matrix was presented. Simulations produced with the model were compared to the measurements reported by Colombo et al. [21], Bettini et al. [22] and Colombo et al. [23]. However the model could not describe the continued swelling of the matrix, subsequent to the disappearance of the swelling front. Models of drug release from hydrogel based matrices of HPMC were presented by [24].

The effect of polymer relaxation constant on water uptake and drug release was shown in a mathematical model for the simulation of water uptake by and drug release from homogeneous poly-(vinyl alcohol) hydrogel [9]. Another work showed that swelling of the hydrogel carrier begins from the edge to the center. At the beginning the drug release is by anomalous transport followed by Fickian diffusion when the swelling of the hydrogel approaches to a new equilibrium state [25].

A mathematical model was developed to describe the transport phenomena of a water-soluble small molecular drug (caffeine) from highly swellable and dissoluble polyethylene oxide (PEO) cylindrical tablets [26]. The work considered several important aspects in drug release kinetics such as swelling of the hydrophilic matrix and water penetration, three-dimensional and concentration-dependent diffusion of drug and water, and polymer dissolution. In vitro study of swelling, dissolution behavior of PEOs with different molecular weights and drug

release were carried out. When compared with experimental results, this theoretical model agreed with the water uptake, dimensional change and polymer dissolution profiles very well for pure PEO tablets with two different molecular weights. Drug release profiles using this model were predicted with a very good agreement with experimental data at different initial loadings. The overall drug release process was highly dependent on the matrix swelling, drug and water diffusion, polymer dissolution and initial dimensions of the tablets. When their influences on drug release kinetics from PEO with two different molecular weights were investigated, it was found that swelling was the dominant factor in drug release kinetics for higher molecular weight of PEO ( $M_w=8 \times 10^6$ ) while both swelling and dissolution were important to caffeine release for lower molecular weight PEO ( $M_w=4 \times 10^6$ ). It was found that when initial drug loading increases, polymer dissolution became more and more important in the release process. Besides swelling and dissolution properties of polymer, the ratio of surface area to volume and the aspect ratio of initial tablets were found to be influential in the overall release profile.

A novel method was developed by [27] to simulate polymer swelling and dissolution by combining a discrete element method (DEM) with inter-particle mass transfer. The method was applied to simulate the behavior of cylindrical tablets. The model considered the effects of several parameters such as the concentration-dependent diffusion constant of water in polymer, dissolution rate constant of polymer and the disentanglement threshold of polymer on the tablet behavior. A new drug component was included in the DEM method and the effects of drug distribution, maximum swelling ratio of polymer and drug-polymer diffusivity on the tablet behaviour were studied [28]. The model was able to explicitly define the drug distribution in the tablet. The model showed that for a homogeneously dispersed drug, the release was slow over time, but for a heterogeneous distribution, there was an initial burst release followed by a slower release.

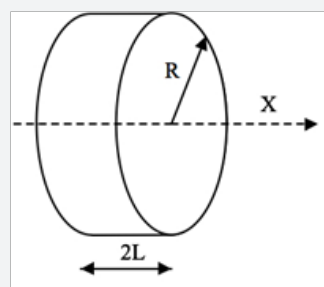
### Approach

#### Proposed Dissolution Model

We employed and adapted the Dissolution Model of [11,29,30]. The model explains the release of a water soluble, crystalline drug enclosed within a swellable, hydrophilic glassy polymer, placed in contact with water or a biological fluid. It is a moving boundary problem formulated using a system of partial differential equations (PDE's) and ordinary differential equations (ODE's) which describe,

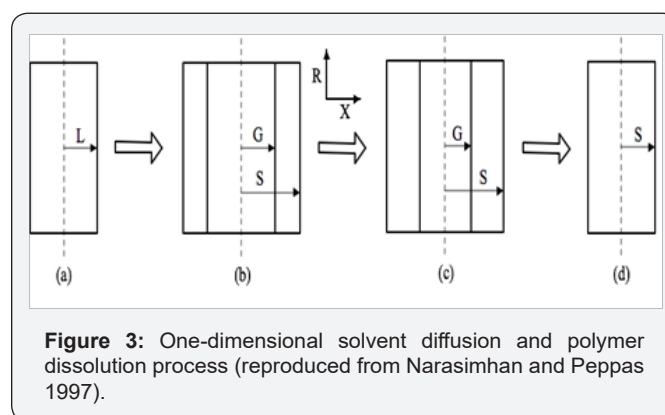
- I. Diffusion of water in to the system;
- II. Diffusion of drug out of the system;
- III. Polymer chain disentanglement through the boundary layer and

IV. The left and right moving boundaries. All the diffusion processes take place along the tablet thickness indicated by  $X$  (Figure 2) making it a 1-D problem in space.



**Figure 2:** Schematic of the drug tablet of initial radius  $R$  and initial thickness  $2L$ .

In this model, when water comes in contact with the glassy polymer of initial thickness  $2L$  (Figure 3a), the polymer starts to swell and two distinct fronts are formed: the swelling interface at position  $G$ , and the polymer-water interface at position  $S$  (Figure 3b). Initially, the front  $G$  moves inwards since the drug starts diffusing out of the gel layer and the front  $S$  moves outwards due to polymer swelling. When the concentration of water inside the polymer gel layer exceeds a critical value  $v_1^*$ , polymer disentanglement begins and  $S$  starts to diminish. Hence, during the latter stage of the dissolution process, both  $G$  and  $S$  move towards the center of the tablet (Figure 3c). The process continues, till the glassy core disappears and only the front  $S$  exists, which continues to diminish till the entire polymer is dissolved (Figure 3d). A detailed description of the various equations used in the modelling of the dissolution model is given below.



**Figure 3:** One-dimensional solvent diffusion and polymer dissolution process (reproduced from Narasimhan and Peppas 1997).

Water transport into the polymer matrix is expressed using Fick's law as:

$$\frac{\partial v_1}{\partial t} = \frac{\partial}{\partial x} \left( D_1 \frac{\partial v_1}{\partial x} \right) \quad G < x < S \quad (3)$$

Where,  $v_1$  is the volume fraction of water in the swollen polymer,  $D_1$  is the diffusion coefficient of water in polymer and  $x$  is dimension along the tablet thickness. Eq. 3 is valid in the slab

region between G and S (Figure 3b & 3c). The diffusion of drug out of the polymer is given by:

$$\frac{\partial v_d}{\partial t} = \frac{\partial}{\partial x} \left( D_d \frac{\partial v_d}{\partial x} \right) \quad G < x < S \quad (4)$$

Here,  $v_d$  is the volume fraction of drug in the swollen polymer and  $D_d$  is the drug diffusion coefficient in the polymer. Eq. 3 and 4 describe the overall swelling/dissolution/release process and are solved with the following initial conditions.

$$v_1(x, 0) = 0 \quad v_d(x, 0) = v_{d0} \quad (5)$$

The first boundary condition for Eq. 3 and 4 is at the glass-rubbery interface, given by:

$$v_1(G, t) = v_1^* \quad v_d(G, t) = v_d^* \quad (6)$$

The critical volume fractions of water and drug at the interface, G, are  $v_1^*$  and  $v_d^*$ , respectively. Here  $v_1^*$  and  $v_d^*$  are functions of the thermodynamic conditions of glassy-rubbery transition, given by:

$$v_1^* = 1 - v_2^* - v_d^* \quad (7)$$

$$v_2^* = \frac{1}{\frac{1}{\rho_2} + \frac{(T_g - T)}{1} + \frac{1}{\rho_1}} \quad (8)$$

$$v_d^* = \frac{\rho_2 - (\beta / \alpha_f) \rho_1 - \rho_d}{\frac{1}{\rho_2} + \frac{(T_g - T)}{1} + \frac{1}{\rho_1} + \frac{1}{\rho_d}} \quad (9)$$

Where,  $T_g$  is the glass transition temperature, T is the experimental temperature,  $\alpha_f$  is the linear expansion coefficient of the polymer,  $\beta$  is the expansion coefficient contribution of water to polymer,  $\rho_1$  is the water density,  $\rho_2$  is the polymer density and  $\rho_d$  is the drug density. The second boundary condition for Eq.3 and 4 is at the rubbery-solvent interface, S, given by:

$$v_1(S, t) = v_{1,eq} \quad v_d(S, t) = v_{d,eq} \quad (10)$$

Where,  $v_{1,eq}$  and  $v_{d,eq}$  are the equilibrium volume fractions of water and drug, estimated using the Flory-Rehner equation (Paul J. Flory 1943).

A mass balance at the interface G gives the moving boundary condition at the glassy-rubbery interface:

$$(v_1 + v_d)_{(G,t)} \frac{dG}{dt} = - \left( D_1 \frac{\partial v_1}{\partial x} \right)_{(G,t)} - \left( D_d \frac{\partial v_d}{\partial x} \right)_{(G,t)} \quad (11)$$

The initial condition for Eq. 11 is given by,  $G(0) = L/2$ , where L is the initial half thickness of the tablet. The values of  $v_1^*$  and  $v_d^*$  at interface G are given by Eq. 6. A mass balance at the interface S gives the moving boundary condition at the water-rubbery interface:

$$(v_1 + v_d)_{(S,t)} \frac{dS}{dt} = - \left( D_1 v_1 \frac{\partial v_1}{\partial x} \right)_{(S,t)} - \left( D_d v_d \frac{\partial v_d}{\partial x} \right)_{(S,t)} - \left( D_p \frac{\partial v_2}{\partial x} \right)_{(S,t)} \quad (12)$$

The initial condition for Eq. 12 is given by,  $S(0) = L$ . The values of  $v_1^*$  and  $v_d^*$  at interface are given by Eq. 10.

As the polymer chains disentangle, they move out of the gel layer through a diffusion boundary layer (semi-dilute regime) of thickness  $\delta_b$ . The polymer chain transport through this boundary layer is given by:

$$\frac{\partial v_2}{\partial t} = \frac{\partial}{\partial x} \left( D_p \frac{\partial v_2}{\partial x} \right) - \left( \frac{dS}{dt} \right) \frac{\partial v_d}{\partial x} \quad S < x < S + \delta_b \quad (13)$$

The initial and boundary conditions to Eq. 13 are given by:

$$v_2(x, 0) = 0 \quad (14)$$

$$v_2(S + \delta_b, t) = 0 \quad (15)$$

$$-D_p \frac{\partial v_2}{\partial x} \Big|_{(S^+, t)} = 0 \quad 0 < t < t_{rept} \quad (16)$$

$$-D_p \frac{\partial v_2}{\partial x} \Big|_{(S^+, t)} = k_d \quad t_{rept} \leq t < t_c \quad (17)$$

$$v_2 \Big|_{(S^+, t)} = v_{2,eq} \quad t_c \leq t \quad (18)$$

Where,  $t_{rept}$  is the reptation time defined as the minimum time taken by the polymer chains to disentangle,  $k_d$  is the polymer chain disentanglement rate and  $t_c$  is the critical time at which polymer concentration in the boundary layer reaches an equilibrium value,  $v_{2,eq}$ .

## Solution Strategy

We developed a step-by-step algorithm to solve the dissolution model equations as described below:

Step 0: Initialization

Step 1: Let  $\epsilon$ , where  $\epsilon$  a small positive number is. Solve the approximated versions of Eq. 11 and 12 simultaneously given by:

$$(v_1^* + v_d^*) \frac{dG}{dt} = - \frac{D_1}{(S-G)} [v_{1,eq} - v_1^*] - \frac{D_d}{(S-G)} [v_{d,eq} - v_d^*] \quad (19)$$

$$(v_{1,eq} + v_{d,eq}) \frac{dS}{dt} = \frac{v_{1,eq} D_1}{(S-G)} [v_{1,eq} - v_1^*] + \frac{v_{d,eq} D_d}{(S-G)} [v_{d,eq} - v_d^*] - k_d \quad (20)$$

Obtain the new  $G$  and  $S$  values

Step 2: Solve Eq. 3, 4 and 13 using the new G and S values obtained from Step 1

Step 3: Solve Eq. 11 and 12 simultaneously (check for  $G > 0$  every iteration, because when  $G = 0$ , we have to solve only Eq. 12)

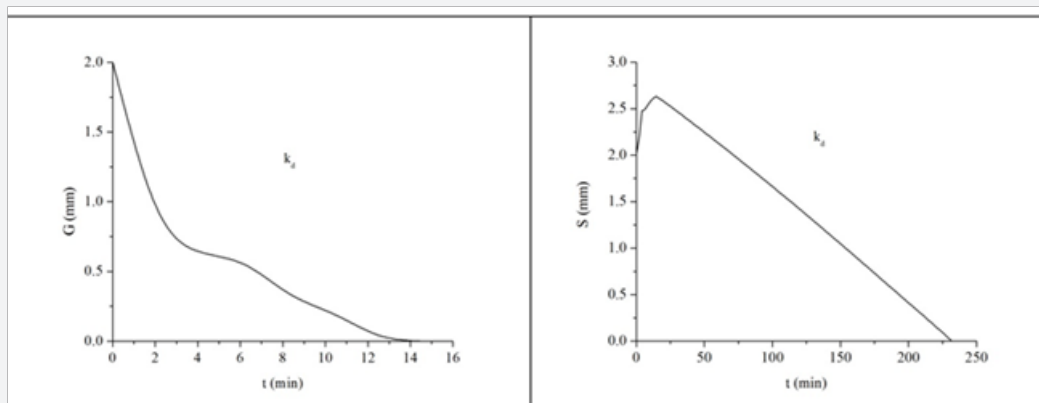
Step 4: If  $S > 0$ , go to Step 2

## Results and Discussion

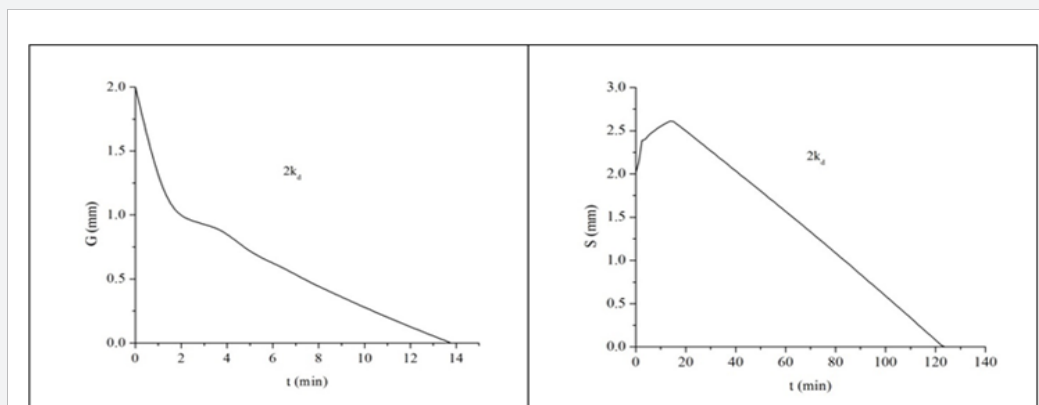
We successfully solved the dissolution model using the modified strategy. The solution is divided into two parts. The first part of the solution includes solving for both G and S until the value of G (thickness of the solid drug tablet) becomes zero. The second part involves solving only for S (thickness of the swollen polymer) after G is zero. Here the contribution of water diffusion to the swelling of the polymer is negligible, only including the drug diffusion and the polymer disentanglement terms resulting in diminishing of S.

We first studied the effect of polymer disentangle rate constant ( $k_d$ ) on the rate at which the tablet dimensions G and S vary inside the body. The value of  $k_d$  has been varied by different factors and plotted curves showing the rate of change

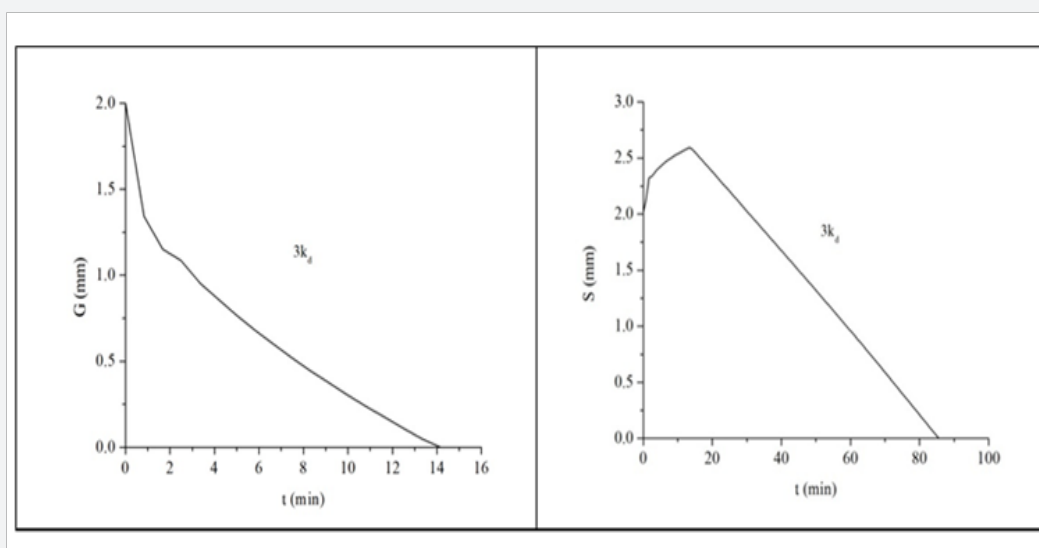
of G and S with time. (Figure 4-7) show the rate of change of G and S with increasing  $k_d$  values of 0.012, 0.024, 0.036 and 0.048 mm/min, respectively.



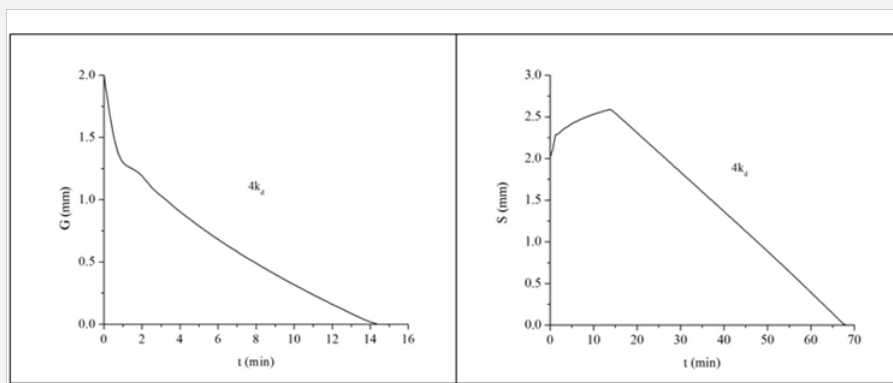
**Figure 4:** Rate of change in tablet interface dimensions G and S for  $k_d = 0.012$  mm/min.



**Figure 5:** Rate of change in tablet interface dimensions G and S for  $k_d = 0.024$  mm/min.



**Figure 6:** Rate of change in tablet interface dimensions G and S for  $k_d = 0.036$  mm/min.

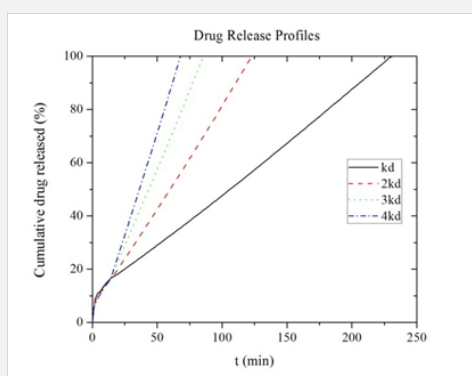


**Figure 7:** Rate of change in tablet interface dimensions G and S for  $k_d$  value of 0.048 mm/min.

Here G is a measure of the solid tablet thickness and S is a measure of the total tablet thickness along with the swollen polymer. An expected trend is observed both in the case of G and S as discussed in section 2.3. The solid tablet thickness (G) decreases with time as the tablet traverses through the GI tract and comes into contact with the bodily fluid. This is due to the continuous diffusion of drug out of the solid tablet and the conversion of solid polymer in the tablet to rubbery (swollen) form. The total tablet thickness (S) initially increases with time because of the polymer swelling and then eventually falls after the concentration of polymer in the gel layer reaches the critical limit and the polymer starts degrading from the tablet.

We observed that, in each of the profiles containing a change in  $k_d$ , there is initial time period of fast decrease rate in the value

of G followed by a relatively slower decrease rate. However, with increase in the  $k_d$  value, there is a noticeable drop in the time period for rapid decrease of G. This initial rapid fall in the value of G can be attributed to the initial burst release of the drug from the tablet. With increasing  $k_d$  value, there is a much faster burst release, leading to decrease in the time for burst release. The change in  $k_d$  value did not have much impact on the total time taken for the solid part of the tablet to dissolve. This is because the dissolution of the solid drug tablet is independent of the polymer disentanglement rate. We observe that with increase in the  $k_d$  value, there is a significant drop in the total time for dissolution of the drug tablet including the swollen gel layer (looking at the trends for change of S), which is expected.



**Figure 8:** Effect of polymer degradation rate constants ( $k_d$ ) on cumulative (%) drug released. The total amount of drug released for each of the  $k_d$  values is a constant of 400 mg.

We have plotted the drug release profiles for different values of  $k_d$ , i.e., the cumulative (%) mass of drug released with time respect to the time of release (t) as shown in Figure 8. The total amount of drug released in each of these profiles is 400mg. Each of the release profiles showed an initial burst release followed by a constant release. This can be clearly observed in Figure 8, where each of the curves has a constant slope after a certain initial burst release, indicating a constant rate of drug release.

We have plotted the rate of drug release (dM/dt) for

different values of  $k_d$  to more clearly observe the burst effect followed by the constant release (Figure 9). We observed that, the burst effect is faster with increase in the  $k_d$  value i.e., the time taken for initial burst release is lower for higher  $k_d$  values. This could indicate that the burst effects can be controlled by varying the  $k_d$  value accordingly. The area under the curve values for each of the curves in Figure 9 is a constant value of 400mg, indicating that a constant amount of drug is released for different  $k_d$  values.

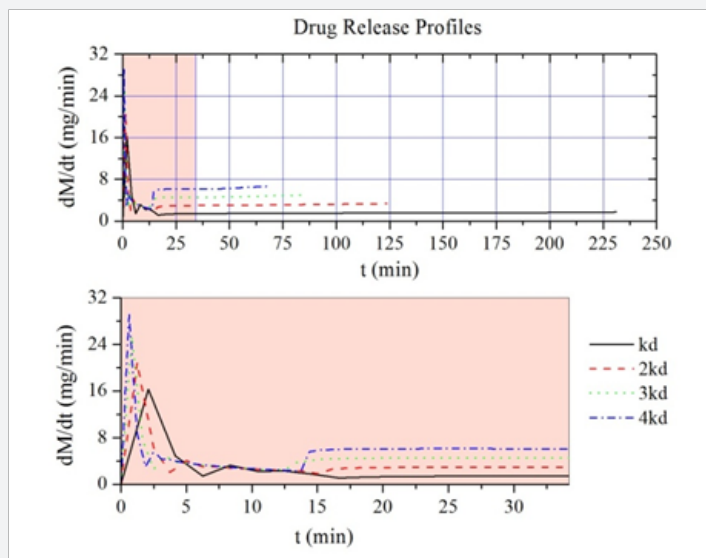


Figure 9: Effect of polymer degradation rate constants ( $k_d$ ) on drug release rate (dM/dt).

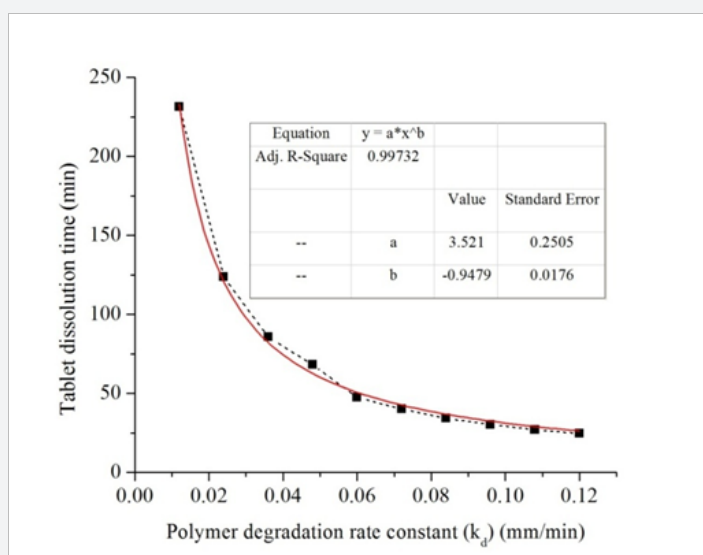


Figure 10: Effect of polymer degradation rate constant ( $k_d$ ) on the tablet dissolution time.

We studied the effect of polymer degradation rate constant ( $k_d$ ) on the total dissolution time of the tablet. Table 1 shows the various tablet dissolution times obtained when the value of  $k_d$  is changed by an increasing factor from 1 to 10. As expected, with increase in the  $k_d$  value, there was a drop in the total dissolution time. This is because, as the value of  $k_d$  increases, the polymer in the tablet dissolves at a much faster rate leading to a drop in the total dissolution time. We observed a dependence of the total degradation time on  $k_d$  followed a smooth trend (Figure 10). Hence we tried to fit a classical Freundlich equation to the data obtained in Table 1.

The classical Freundlich equation (power law) is of the form given in Eq. 21.

$$y = ax^b \tag{21}$$

Where,  $y$  is the total tablet dissolution time in our case and  $x$  is the polymer degradation rate constant ( $k_d$ ), and  $a$  and  $b$  are the parameters that are estimated to fit the data. The results are given the classical Freundlich equation was an excellent fit to the data with an  $R^2$  value of 0.997 as shown in Figure 10. This correlation between the tablet dissolution time and polymer degradation rate constant is very useful, since we will be able to estimate the dissolution times of a tablet without experimental data. We will be able to determine the type of polymer required to make the tablet in order to obtain a desired tablet dissolution time.



## Conclusion

We successfully developed a drug release model by modifying a dissolution model proposed by [31]. The developed model can be used to predict the release behavior of an oral drug from the solid drug tablet inside the GI tract of the body. A solution strategy is proposed to solve the moving boundary problem encountered in solving the drug release model. Using this model, we studied the effects of model parameters such as the polymer degradation rate constant ( $k_d$ ), on the tablet dissolution rate. We specifically studied the effect on the thickness of the solid tablet ( $G$ ) as well as the total tablet including the swollen gel layer ( $S$ ). The value of  $S$  continuously decreased with time, while the value of  $S$  initially increased and then decreased as expected. The profiles indicated a burst release during the initial stages of the release process.

We studied the effect of  $k_d$  on the total tablet dissolution time. There was a significant drop in the tablet dissolution time with increase in the  $k_d$  value. We fit a classical Freundlich equation to estimate the tablet dissolution time with change in  $k_d$  value. The obtained correlation could be very beneficial in estimating the tablet dissolution time without the need of any experimentation, as well as to estimate the  $k_d$  value for a desired tablet dissolution time. The model predicted the initial burst release of the drug followed by a constant release.

The solution which we have employed in this model to solve the moving boundary problem is an approximate solution. There is need of a more improved and continuous solution to the moving boundary problem which will help us to make more accurate predictions. One more major assumption in our model is that the drug release takes place only along the tablet thickness (axial direction). Hence it is a 1-D model. A model considering the release in all the directions is desired (a 2-D model). The model solution strategy employed in this paper is a discretized approach, where the time and space are divided in small fractions and the model is solved in each of these fractions. We need a much better solution which is more continuous and give a more accurate representation of the drug release process.

The developed model will provide insights into the various mass transport, diffusion and degradation processes involved in the mechanism of drug release from a swelling polymer matrix. This model will greatly aid in simulating some of the in vitro dissolution tests and reduce the number of experiments, and hence reduce the time and effort involved.

## Nomenclature

- $L$  : Initial half thickness of the drug tablet
- $v_1$  : Volume fraction of water in the swollen polymer
- $v_d$  : Volume fraction of drug in the swollen polymer
- $v_1^*$  : Critical volume fraction of water at the interface
- $v_d^*$  : Critical volume fraction of drug at the interface

- $v_{1,eq}$  : Equilibrium volume fraction of water
- $v_{d,eq}$  : Equilibrium volume fraction of drug
- $v_{d0}$  : Initial volume fraction of the drug
- $T_g$  : Glass transition temperature
- $T$  : Experimental temperature
- $\alpha_f$  : Linear expansion coefficient of the polymer
- $\beta$  : Expansion coefficient contribution of water to polymer
- $\rho_2$  : Polymer density
- $\rho_d$  : Drug density
- $D_1$  : Diffusion coefficient of water in polymer
- $D_d$  : Diffusion coefficient of drug in polymer
- $k_d$  : Polymer chain disentanglement rate

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