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Diffusional release of a dispersed solute from a cylindrical polymeric matrix into an infinite external volume

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ABSTRACT

Numerical and analytical exact solutions of diffusional release from a cylindrical polymeric matrix into an infinite medium have been developed in which the initial solute loading (A) is greater than solubility limit (C_s). Also, the effects of boundary layers on the drug release rate have been studied. The numerical solution is valid for any initial drug loading whereas analytical solution can be used for high values of drug loading. Comparisons have been made between numerical and analytical exact solutions in upper and lower bounds ($A/C_s \gg 1$ and $A/C_s \to 1$) and previously presented approximate solution. The presented results validate the proposed numerical solution.

1. Introduction

The theoretical description of a solute release from a polymeric matrix when the initial drug loading (A) is greater than the solubility limit (C_s), is a matter of interest in controlled release drug delivery. The drug release from such matrix is mainly controlled by diffusion process [1]. These systems should be modeled by considering a moving diffusional front separating the core, which is intact region, and the partially extracted region. An approximate solution for diffusional controlled release from the matrix with planar and spherical geometries was developed by Higuchi [2,3]. This model was based on the pseudo-steady state assumption that is applicable in the lower diffusional front velocity thus; its accuracy decreased in lower drug loading. Lee [4] exerted the refined integral method to develop an approximate solution for drug release from the matrix with planar and spherical geometries. Paul and McSpadden's [5] presented an exact solution for the slab geometry. A generalized approximate solutions for dissolution/diffusion controlled release systems have been presented by Xiang and McHugh [6] and Cabrera and Grau [7]. Using combination of variables, Abdekhodaie and Cheng [8–10] developed an exact solution for solute release from a spherical polymer matrix into both finite and infinite external medium. With this approach, Fick's second law reduces into an ordinary differential equation. Exact solution for drug release from a cylinder into an infinite well agitated medium when initial drug loading is less than its solubility in the polymer was demonstrated by Crank [11] and Fu [12].

Zhou and Chu [13] developed a pseudo-steady state analysis for drug release from two dimensional matrix tablets. Frenning and Brohede [14] presented a model for drug release from a cylindrical matrix into a well-mixed medium using finite element method. Shefeeq and Ahmad presented a model for solute release from a cylindrical polymer matrix into a finite external volume by combination of variables which is mathematically not correct [15]. Roseman–Higuchi [16]

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developed an approximate solution for drug release from a dispersed cylindrical system. This model based on pseudo-steady state assumption that is only applicable for higher drug loadings.

The present study intends to develop an exact solution as well as an easily applicable numerical solution for diffusional release of a dispersed solute from a cylindrical polymeric matrix into an infinite external volume with and without boundary layer effects. In addition, comparisons between exact and numerical solution and previously presented approximate solution will be made.

2. Analysis

The diffusional release of a dispersed solute from a polymeric matrix with cylindrical geometry into an infinite medium is considered. The diffusion coefficient is assumed to be independent of concentration. In addition, solute diffusion is assumed to be the rate controlling step rather than polymeric swelling or drug dissolution. In fact, in the systems that are accompanied by little swelling or experience rapid swelling relative to solute diffusion, the diffusional release occurs from a pre-swollen polymer so, the polymer swelling kinetics can be neglected. Solute release from end-sides of cylinder is neglected and the problem has been solved for two situations: (a) External mass transfer resistance was neglected. (b) An external mass transfer resistance was considered in a form of a boundary layer.

The drug distribution in the cylinder after a certain time of release is illustrated in Fig. 1.

Cylindrical matrix consists of two regions: the surface zone, $R < r < S$ in which all solute is dissolved and the core region $0 < r < R$, which contains undissolved solute. S corresponds to the radius of a cylindrical matrix. The two zone are separated by the diffusion front, $r = R$, which moves inward as time progress. The concentration is essentially constant in an unextracted region, $0 < r < R$, while the concentration in the partially extracted region, $R < r < S$, is a function of both time and the position and is determined by transient diffusion according to Fick's second law:

$$\frac{\partial C}{\partial t} = \frac{D}{r}\frac{\partial}{\partial r}\left(r\frac{\partial C}{\partial r}\right) \tag{1}$$

where D is the diffusion coefficient and C is the concentration of dissolved solute in the matrix. The initial and boundary conditions are:

$$R[t = 0] = S \tag{2}$$

$$C[R(t), t] = C_s \tag{3}$$

$$D\frac{\partial C}{\partial r} = (A - C_s)\frac{dR}{dt} \quad \text{at } r = R(t) \tag{4}$$

where A is the initial solute loading per unit volume and C_s is the solubility limit of the solute in the matrix. Eq. (2) states that the initial position of the diffusion front is at the matrix surface. Eq. (3) states that at the diffusion front, the solute concentration is equal to its solubility in the matrix; this statement can be viewed as a definition of the diffusion front. Eq. (4) describes the mass balance at the diffusion front. When a perfect sink condition without an external mass transfer resistance is considered the boundary condition at the surface becomes

$$C[S, t] = 0 \tag{5}$$

When an external mass transfer resistance exists in a form of boundary layer, the boundary condition at the surface is

$$-D\frac{\partial C}{\partial r} = h(C_\infty - 0) \quad \text{at } r = S \tag{6}$$

where h is the mass transfer coefficient in boundary layer and C_∞ is the external concentration at the surface. Assuming equilibrium between the matrix surface and the external fluid at the surface Eq. (6) becomes:

$$-D\frac{\partial C}{\partial r} = \frac{hC}{P} \quad \text{at } r = S \tag{7}$$

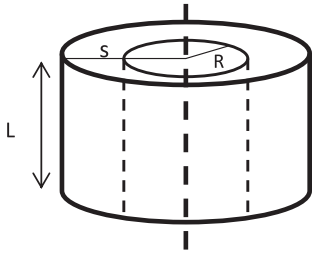

Fig. 1. Schematic diagram of partially extracted matrix with cylindrical geometry: R, position of moving diffusion front; S, position of cylinder surface.