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TITLE OF THE THESIS: A MATHEMATICAL STUDY ON DRUG RELEASE MECHANISM FROM CONTROLLED RELEASE SYSTEM

ABSTRACT

Controlled drug delivery has been attracting a great deal of attention in the medical community for years as an efficient way of providing treatment for a wide class of diseases. However, the development of advanced drug delivery can be facilitated through mathematical modeling of controlled release systems. Mathematical modeling of controlled drug delivery phenomena plays a pivotal role in designing new controlled drug delivery systems. An adequate model may be helpful to predict drug release rate from and drug diffusion through polymers avoiding excessive experimentation; furthermore, by comparison of release data and modeling simulations it may be possible to establish the mechanism of drug release and to provide more general guidelines for developing other systems.

This thesis is focused on studying the drug release kinetics from cylindrical release systems by using mathematical modeling techniques. We address the problem by taking different cases of the cylindrical delivery system. The model equations were derived by using different methods. The drug release were studied in radial direction only. The behavior of fractional release and the dependence of different parameters on drug release were also investigated.

In **Chapter 1,** an overview of the problem has been given by considering both drug delivery and mathematical modeling aspects. **Chapter 2** presents an exact solution for the release kinetics of a solute from a cylindrical reservoir into a finite external volume. The cumulative and fractional solute release profiles have been calculated for different external volumes. The results presented indicate that, as the external fluid volume increases, the cumulative and fractional release of the solute at any time increase. The results of this chapter have been published in **JMI Int. J. Math. Sci. Vol. 2, 2011**.

Chapter 3 deals with the analytical treatment of diffusional release of a dispersed solute from a cylindrical non-erodible polymeric matrix system into an infinite sink. The behavior of the fractional solute release, M_t/M_∞, has been studied by using equations for the moving diffusion

boundary and the cumulative solute release. The kinetics of diffusional release of solute from the matrix system as a function of drug loading parameter has also been studied. The obtained results show that the fractional drug release increases with the increasing values of drug loading parameter. Further, the dynamical behaviour of fractional release, M_t/M_∞, of the solute indicates the increase in fractional drug release as a function of τ till a critical time τ_c, beyond which it remains constant showing no release of drug occurs after τ_c. This τ_c found to be as a function of solute loading parameter. The content of this chapter has been published in **J. Nanosci. Nanotechnol. Vol. 12, 2012**.

Chapter 4 describes a mathematical model for the diffusional release of a dispersed solute from a cylindrical polymeric matrix in a perfect sink. Moving boundaries of dispersed drug in radial direction and fractional release kinetics have been calculated for different values of solute loading levels. The obtained results have been compared with available approximate analytical solution. The analysis reveals that the release kinetics of a dispersed solute from a matrix system is significantly influenced by different features of release system such as geometry, initial loading etc. The results of this chapter have been published in **Adv. Sci. Focus, 1, 120-123, 2013.**

The **5th** and **6th Chapters** are devoted to describe dispersed-drug release from cylindrical ensembles into a finite external medium with a boundary layer effect. The analytical solutions have been derived based on pseudo-steady state approximation for the case of $C_0 > C_S$ and $C_0 >> C_S$, where C_0 is the initial drug loading and C_S is the drug solubility in the matrix. The influence of different parameters such as solute loading, coating material and thickness, and external conditions like the liquid volume and boundary layer thickness has been analyzed. A comparison of general and simplified solutions has been conducted. The average amound of drug released, M_t^A, as a function of various parameters has also been simulated. The obtained results reveal the dependence of release kinetics on different parameters and provide a theoretical platform for the design of dispersed drug delivery devices. The results of these chapters have been accepted for publication in **Adv. Sci. Eng. Med., 6, (xx-xx), 2014**. A general conclusion of the present study has been given in **Chapter 7**. The possible applications and future directions of the study have also been briefly discussed.