



Drug solubility character and release from controlled release polymer based matrices: An analysis of front(s) movement on dissolution rate

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Introduction

The earliest studies in the field of modified drug delivery date back to the 1950s. Since then, a large number of drug products, mainly in the form of tablet and capsule with various controlled release characteristics, have been introduced. This incredible growth can be attributed to several advantages that these products offer, including improved patient compliance, better therapeutic efficiency, potential for patentability, and opportunity for extending product life-cycle. Various technologies have been investigated in order to achieve different aims of controlled drug delivery, e.g. sustained, delayed, pulsatile, targeted, and programmed release. Regardless of the delivery type, the main mechanisms associated with drug transport in these systems include diffusion, swelling, erosion, ion exchange, and osmotic effect which have been investigated in several studies. Among different technologies used in controlled drug delivery, hydrophilic matrix systems are still the most popular because of the simplicity of formulation, ease of manufacturing, low cost, FDA acceptance, and applicability to drugs with wide range of solubility (see references). Drug release from these systems is the consequence of controlled matrix hydration, followed by gel formation, textural and rheological dynamics, matrix erosion, and/or drug dissolution and diffusion, the significance of which depends on drug solubility and concentration and changes in matrix characteristics as illustrated in Fig. 1, A and B.

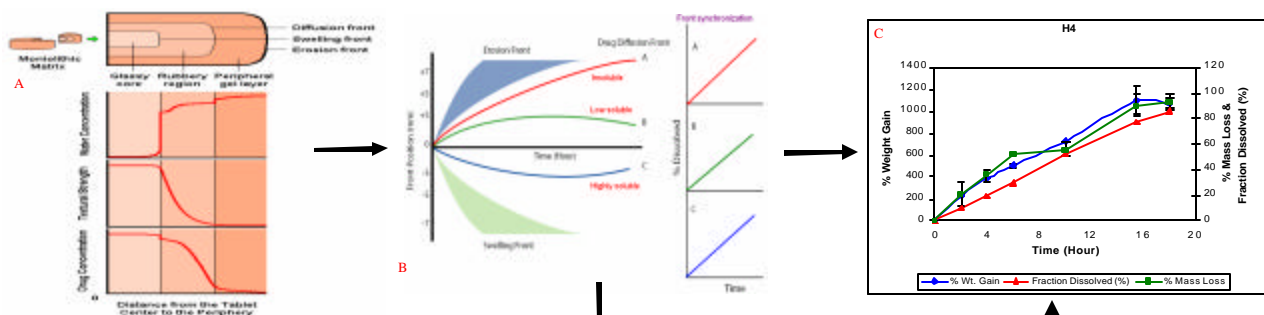


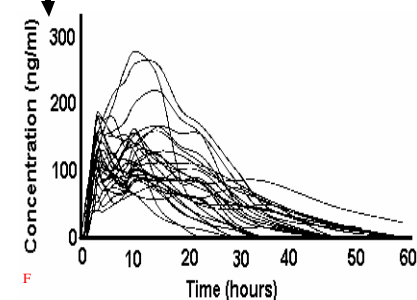
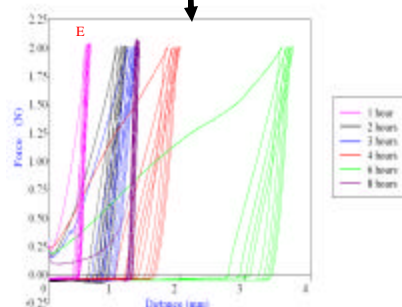
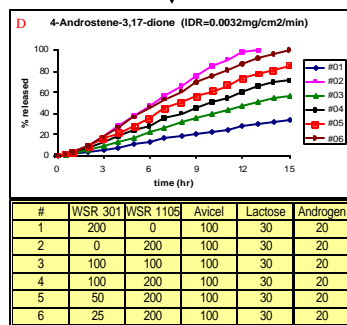
Figure 1. A. Dynamics of swelling and various fronts during drug release from a typical hydrophilic matrix tablet.
B. Position of various fronts for drugs with different solubility and drug release when front synchronization prevails.
C. Zero-order release for glipizide when synchronization of swelling, erosion and particle translocation occurs.
D. Additive influence of polymers on swelling/erosion behavior and release kinetics: Diffusional /Relaxational Ratio
E. Texture Analysis of matrix behavior during dissolution when subjected to controlled and repeated compression.
F Actual blood profiles for 10mg glipizide

Objectives

To analyze influence of various fronts on release mechanisms associated with fenofibrate, 4-androstene-3, 17 dione and glipizide using hydrophilic polymer matrices.

Methodology

Dry blends of various drugs and polymers such as polyoxyethylene, hydroxypropyl methylcellulose, and microcrystalline cellulose, after lubrication were compressed under constant compression force using a Carver press. Tablet properties were determined and their dissolution and textural profiling over 24 hour period determined. For these USP 27 apparatus II (VK 7000, Vankel, Cary, NC) and a texture TA.XT2i analyzer (Texture Tech. Scarsdale, NY / stable Micro System) were used



Results and Discussion

The dynamics of various fronts and drug solubility's within the matrix appear to play in a synchronous manner. Drug release and overall dissolution from various matrices are in accordance with the hydration rate and extent of swelling as determined and illustrated through textural profiling. Type of dissolution profiles for all drugs from the same matrix composition clearly shows the interrelationship between drug solubility and swelling/erosion properties of the polymer. For insoluble drugs fenofibrate, androstene-dione, and glipizide zero-order release rates (over 20 hours) were achieved when proportional changes in polymer concentrations were considered especially in the case of highly swellable and erodible systems.

Conclusions

Results indicate that in the case of drugs with low solubility total drug release in a controlled manner heavily depends on the synchronization of polymer erosion and drug particle translocation fronts. Evaluation of the drug release kinetics and overall dissolution process under stressed conditions mimicking GI contraction forces of up to 2N by subjecting the hydrated matrix to programmed compression forces may provide more reliable data for IVIVC establishment.