

# DRUG DELIVERY SYSTEMS – A Brief Approach

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## 1 Drug delivery systems

Although drug delivery may not attract the attention and press coverage of some of the other disciplines involved in drug discovery, it is an equally important issue in the development of a successful product. Besides the choice of the active drug substance (active pharmaceutical ingredient - API), a responsible decision regarding the route of administration and dosage form needs to be made. A wrong choice can cause failure of therapy. Dosage forms may be classified into:

- Conventional release;
- Modified release which can be delayed, controlled or sustained.

The conventional release dosage forms are designed to release the drug promptly after administration of a bo-

lus for immediate release. In contrast, modified release dosage forms are designed to modulate drug release, delaying or prolonging the dissolution. Various technologies may be employed to promote the gradual release of a drug from a pharmaceutical form.

In the conventional therapy, aliquot quantities of a drug are introduced into the system at specified time intervals resulting in a considerable fluctuation on drug concentration levels. However, an ideal dosage regimen would be the one in which the concentration of the drug is maintained between the limits of the therapeutic window at a constant level throughout all the treatment period. Both situations can be graphically represented in Figure 1.

The basic goal of this kind of therapy is to achieve a steady state blood level that is therapeutically effective and non-toxic for an extended period of time. The design of a proper dosage regimen is an important element when we want to accomplish this objective. An excellent drug delivery system provides the right amount of drug or its active metabolite to the target, at a time and rate that optimizes its effect, without compromising patient safety.

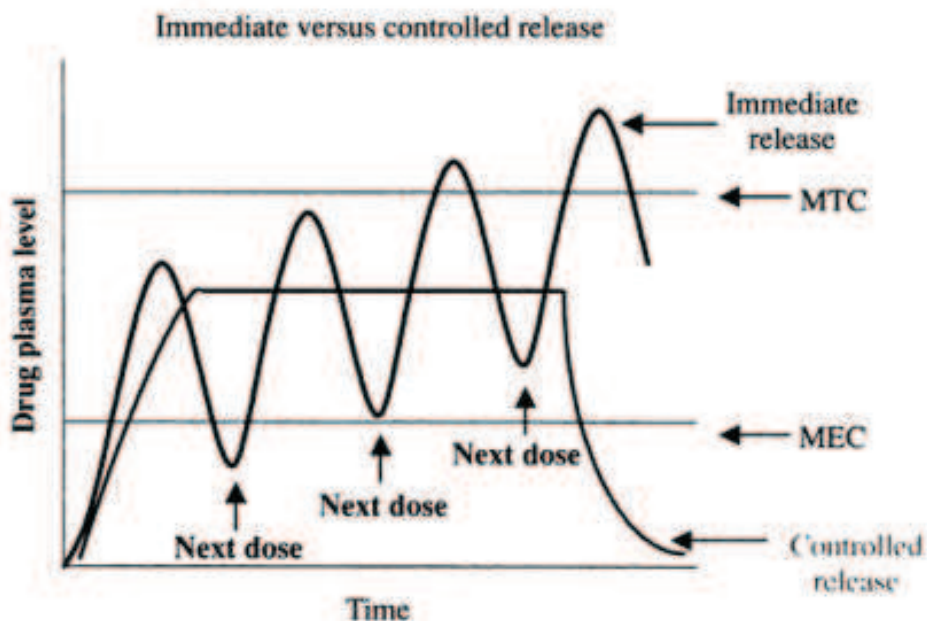


Fig. 1 - Immediate versus controlled release dosage forms.  
(MEC-Minimum effective concentration; MTC-Minimum toxic concentration)

in Steve I. Shen, Bhaskara R. Jasti, and Xiaoling Li, Standard Handbook of Biomedical Engineering and Design, Myer Kutz (ed), Chapter 22: Design of Controlled-Release Drug Delivery Systems, Copyright The McGraw-Hill Companies, Inc. 2003

Controlling release to meet these requirements can involve preventing release or delivery in enzymatically or other hostile environments, targeting a specific location to enhance therapeutic index, or prolonging delivery to sustain an effect. Delivery on demand may also be required with biosensors linked to a delivery device like a drug reservoir, for example. Pros and cons of controlled Drug Delivery Systems (DDS) can be listed as follows:



- Improved patient convenience and compliance due to less frequent drug administration.
- Reduction in fluctuation achieving a steady-state level and therefore better control of disease condition.
- Increased safety margin of the drug due to better control of plasma levels.
- Maximum utilization of drug enabling reduction in total amount of dose administered.
- Reduction in health care cost through improved therapy and shorter treatment period.
- Less frequency of dosing and reduction in personnel time to dispense, administer and monitor patients.
- Better control of drug absorption can be obtained, since the high blood level peaks that may be observed after administration of a single dose corresponding to a high bioavailability drug can be reduced.



- Decreased systemic availability in comparison to immediate release conventional dosage forms; this may be due to incomplete release or insufficient residence time for complete release, for example.
- Poor in-vivo/in-vitro correlation.
- Possibility of dose dumping due to food interaction with formulation and thus increased risk of toxicity.
- Retrieval of drug is difficult in case of toxicity, poisoning or hypersensitivity reaction.
- The physician has less flexibility in adjusting dosage regimens. This is fixed by the dosage form design.
- Economic factors must also be assessed, since more costly processes and equipment are involved in manufacturing many of the sustained release forms.

Medication delivery to the systemic circulation through the skin is an alternative to oral and parenteral routes of administration. The first Transdermal Drug Delivery Systems (TDDS) or drug loaded patches entered the U.S. market in 1979 with the approval of the scopolamine patch by the Food and Drug Administration (FDA) for treatment of motion sickness. Today there are more than twenty different types of medication patches available, and researchers are constantly striving to develop additional and improved methods for transdermal delivery of medications. The great advantage lays on the fact that it avoids first pass metabolism reactions which occur in the liver and gut wall resulting in a decrease on drug bioavailability. TDDS (transdermal patches or transdermal drug delivery systems) are designed to show a perfect adhesion onto healthy and clean skin in order to assure controlled drug delivery into the systemic circulation. Problems linked with factors that affect percutaneous absorption must be studied and solved. This is the purpose of several research teams working in universities all over the world. Actually those problems are connected with the following questions:

- Drug physicochemical properties: solubility, molecular weight, partition coefficient;
- Stratum corneum characteristics like thickness and lipophilicity;
- Concentration of the drug;
- Area of the applied field;
- Drug affinity for the skin.

Some promoters of percutaneous absorption have been suggested. Chemical permeation enhancers, iontophoresis, sonophoresis and even micro or nano needles are good examples. Different types of delivery systems involve different technologies to sustain release and can be listed as shown below:

- Matrix systems: the matrix can be hydrophilic or hydrophobic and drug release processes can involve swelling of the polymer in use, drug diffusion and matrix erosion;
- Reservoir systems;
- Osmotic pumps;
- Other systems – micro or nano sized needle arrays.

The improvement and innovation in the development of controlled release systems strongly depend on select-

ing an appropriate agent capable of controlling drug release. The ideal agents for these preparations should ensure that the drug is released at the right place in the right dose and at (or during) the required time. In addition, it must be said that with the advances in the field of chronobiology, modern drug delivery approaches have been elevated to a new concept of chronopharmacology, which is the ability to deliver the therapeutic agent to a patient in a pulsatile profile. New technology for medications delivering in a time-modulated fashion, by bedside or ambulatory pumps, is being developed to manage human diseases, mainly chronic diseases.

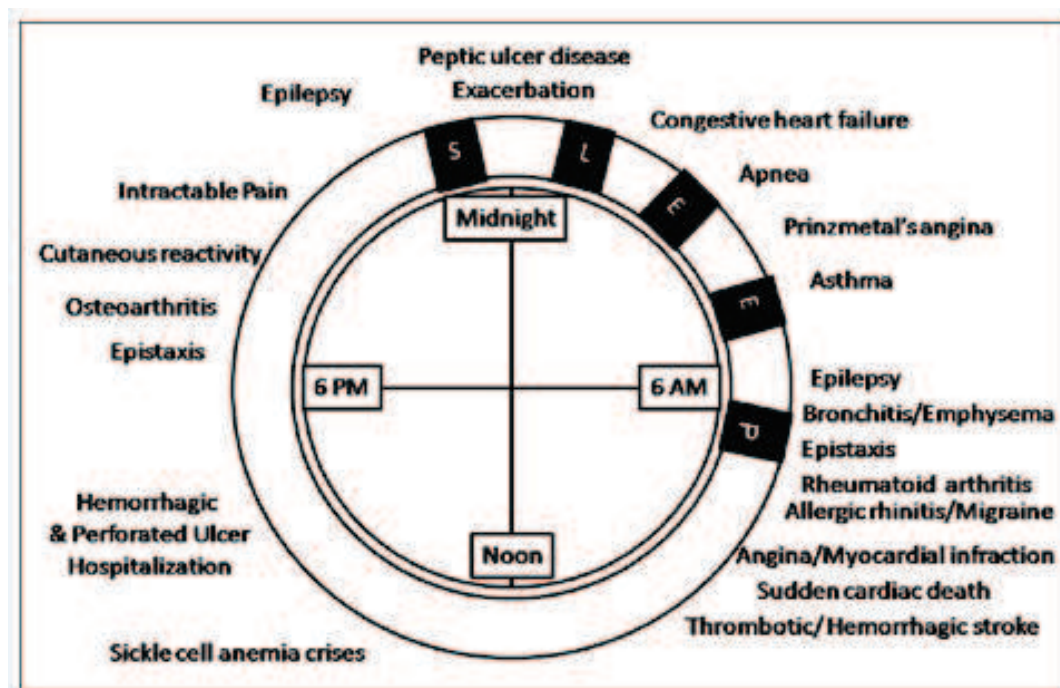


Fig 2 - Time cycle when the diseases show their maximum effect

in Bisht R., Chronomodulated drug delivery system: A comprehensive review on the recent advances in a new sub-discipline of 'chronopharmaceutics'. Asian J Pharm; 2011; 5:1-8

## 2 Controlled Drug Delivery at CDRSP

In our research center, we are trying to “build” a model in which levodopa (3,4-Dihydroxy-L-phenylalanine) is entrapped inside a sodium alginate membrane for skin administration with a controlled mechanism of delivery. It is expected that transdermal route would provide a supply of the drug to the blood stream without fluctuations

on therapeutic levels. This fact is very important in order to avoid the typical on-off effects related to the therapeutics of Parkinson Disease, the disorder in which levodopa is still the gold standard. In our labs, we produce and characterize our drug loaded membranes; then, we carry out the necessary dissolution assays required by the Pharmacopoeias and recommended by the drug national and international authorities. Finally, specific mathematical models are applied in order to understand the drug release mechanism from the polymeric matrix.

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*PONTIAC DEBUTS 2007 SOLSTICE GXP AT LA AUTO SHOW*  
*The GXP version of the Solstice debuted at the Los Angeles Auto Show in January 2006.*

The Pontiac Solstice Coupes are considered to be quite rare: There were a total of 1,266 Solstice Coupes that were able to be manufactured before the production line in Wilmington, Delaware was shut down: 102 pre-production 2009 models, 1,152 sequentially-vin'd regular production 2009 models, and 12 pre-production 2010 models. This is in contrast to over 64,000 of the Pontiac Solstice Convertibles that were manufactured.

— Wikipedia