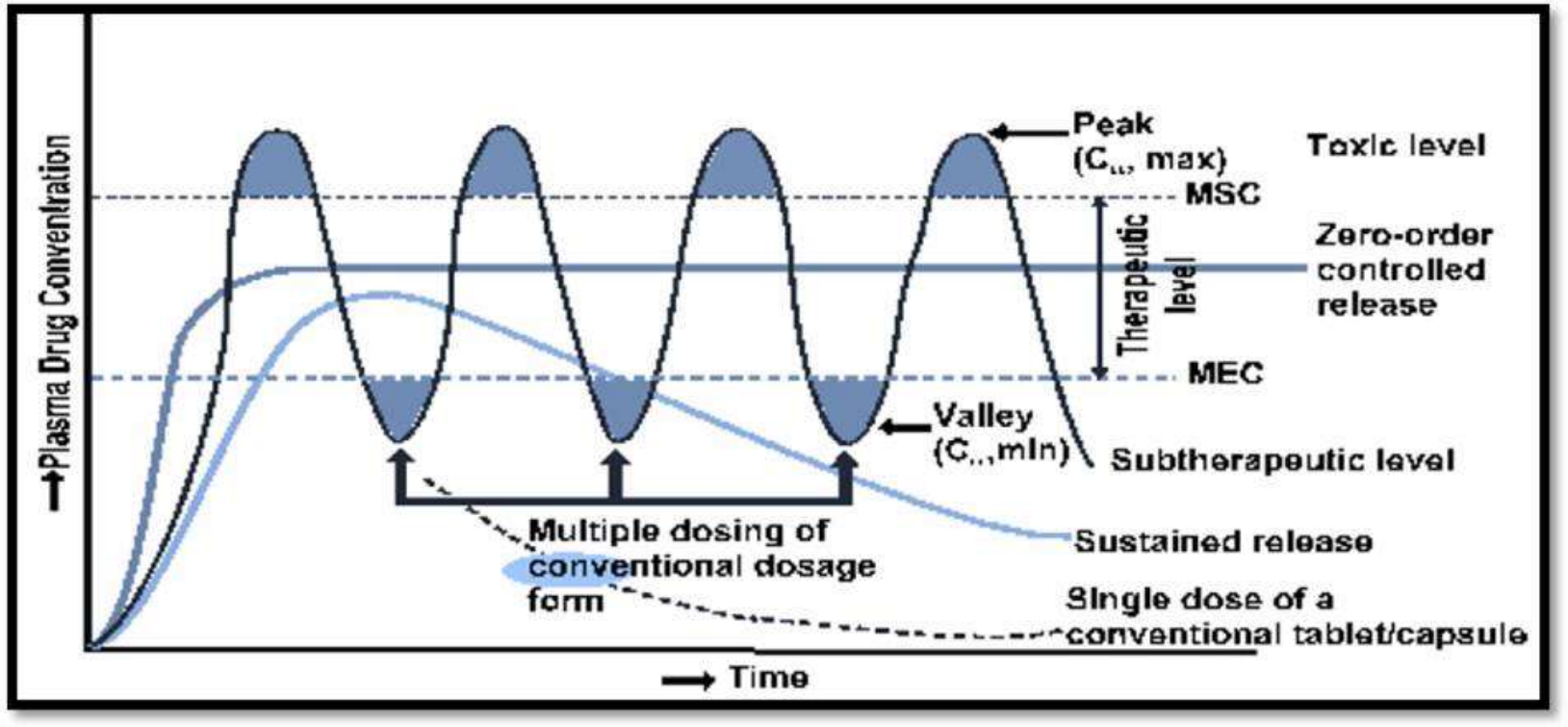
SYSTEMS FOR CONTROLLED DRUG DELIVERY AND DELIVERY MECHANISMS

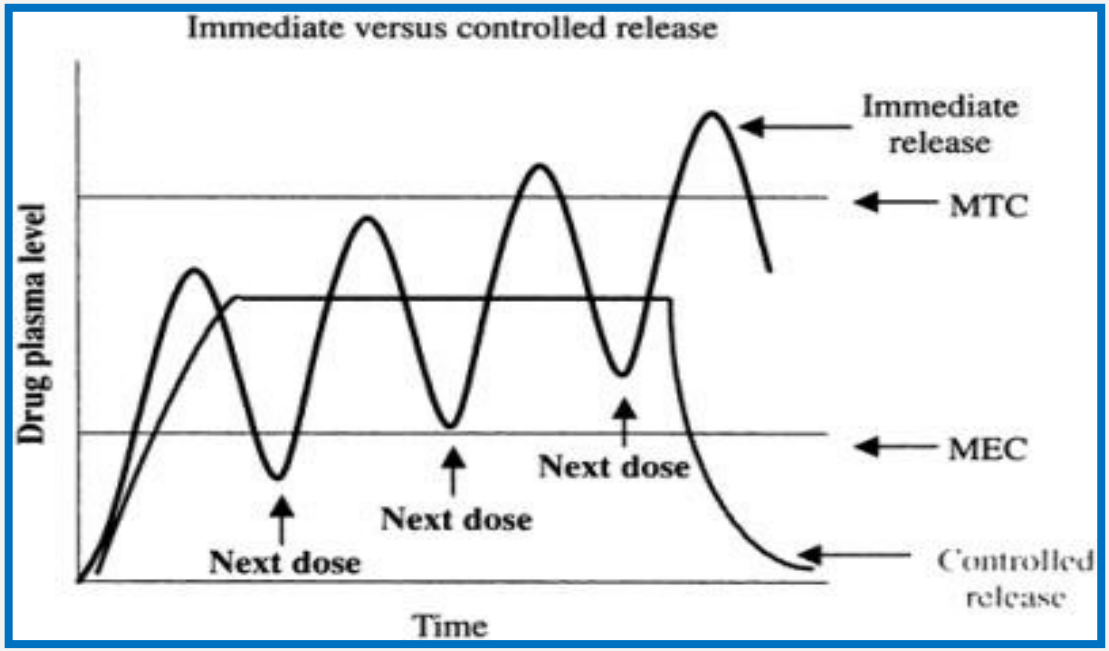
WEEK 1

Conventional dosage forms are designed to release the active agent to ensure immediate and complete systemic absorption.



However, some problems arise with the frequent and repeated administration of such dosage forms:

- the concentration of the active substance may fall below the effective level or
- rise above the toxic level and consequently increase the side effects or their severity.

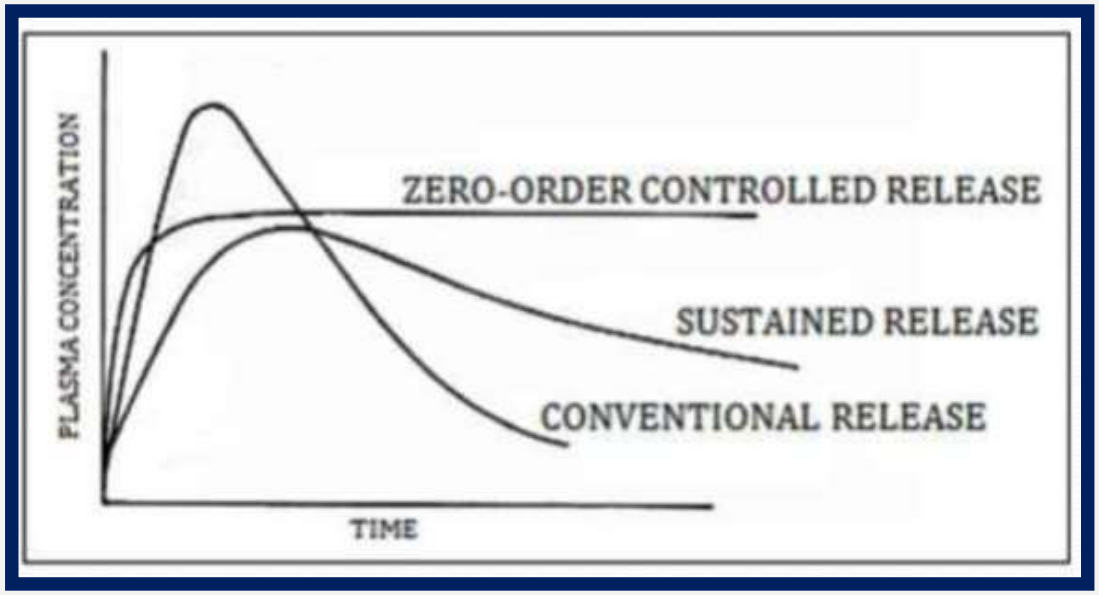


These problems can be overcomed by systems which prolong the systemic absorption and biological activity of the active agents by releasing the active agent over a longer period of time than the immediate release dosage forms.

Controlled drug delivery systems deliver the **drug** at a predetermined rate, for locally or systemically, for a specified period of time.

Controlled drug delivery systems provide modified drug release.

Modified release dosage forms; forms administered by the same route with conventional dosage forms such as solutions, ointments, tablets or capsules but release the active agent at different sites and / or rates than



Therminology

Due to the varying release characteristics, a number of different expressions are used to describe controlled release systems, and different types of classifications are found based on different references.

According to EP 2005, drug release systems are classified as follows:

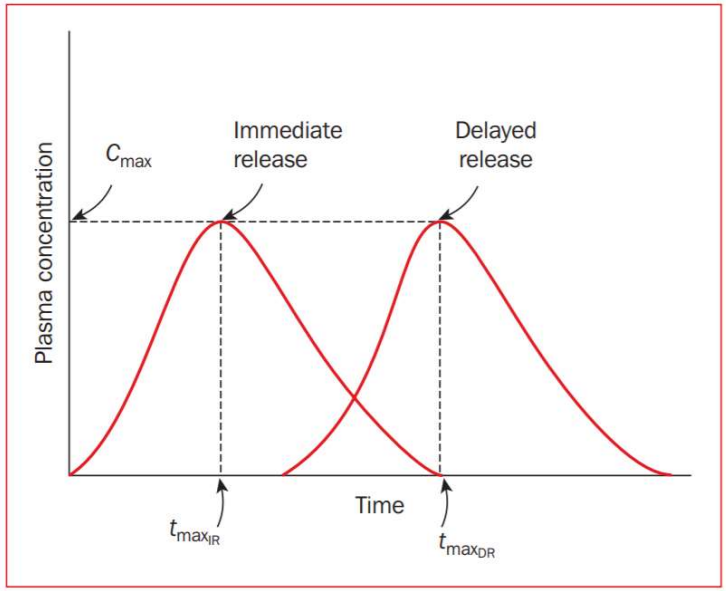
1. Conventional release dosage forms / Immediate release dosage forms
2. Modified release dosage forms
3. Pulsatile release dosage forms
4. Delayed release dosage forms / Gastro-resistant preparations
5. Prolonged release dosage forms / Extended release dosage forms

In USP 27, Modified Release Systems are grouped under two main groups.

1. Delayed release systems
2. Extended/prolonged release systems
   a) Controlled release systems
   b) Sustained release systems

Delayed release: Delayed-release dosage forms can be defined as systems which are formulated to release the active ingredient at a time other than immediately after administration. Delayed release from oral dosage forms can control where the drug is released, e.g. when the dosage form reaches the small intestine (enteric-coated dosage forms) or the colon (colon-specific dosage forms).

Figure 1.3 Idealised plasma concentration versus time profile of a delayed-release oral dosage form compared to an immediate-release dosage form. T_{maxIR} is the time for maximum plasma concentration of the drug released from an immediate-release dosage form and T_{maxDR} is the time for maximum plasma concentration of the drug released from a delayed-release dosage form.



Extended release: Extended-release systems allow for the drug to be released over prolonged time periods. By extending the release profile of a drug, the frequency of dosing can be reduced.(min 2 doses).

Extended release can be achieved using sustained- or controlled-release dosage forms.

Controlled release systems; release rate can be adjusted in advance and drug release fits zero degree kinetics.

Can maintain the plasma or tissue levels of the active substance for a much longer period than conventional dosage forms. However, since the system can be affected by the ambient conditions, it is difficult to determine the release mechanism in advance. In general, drug release fits first order kinetics.

Pulsatile release dosage forms; **modified release systems in which the active agent is released consecutively.**

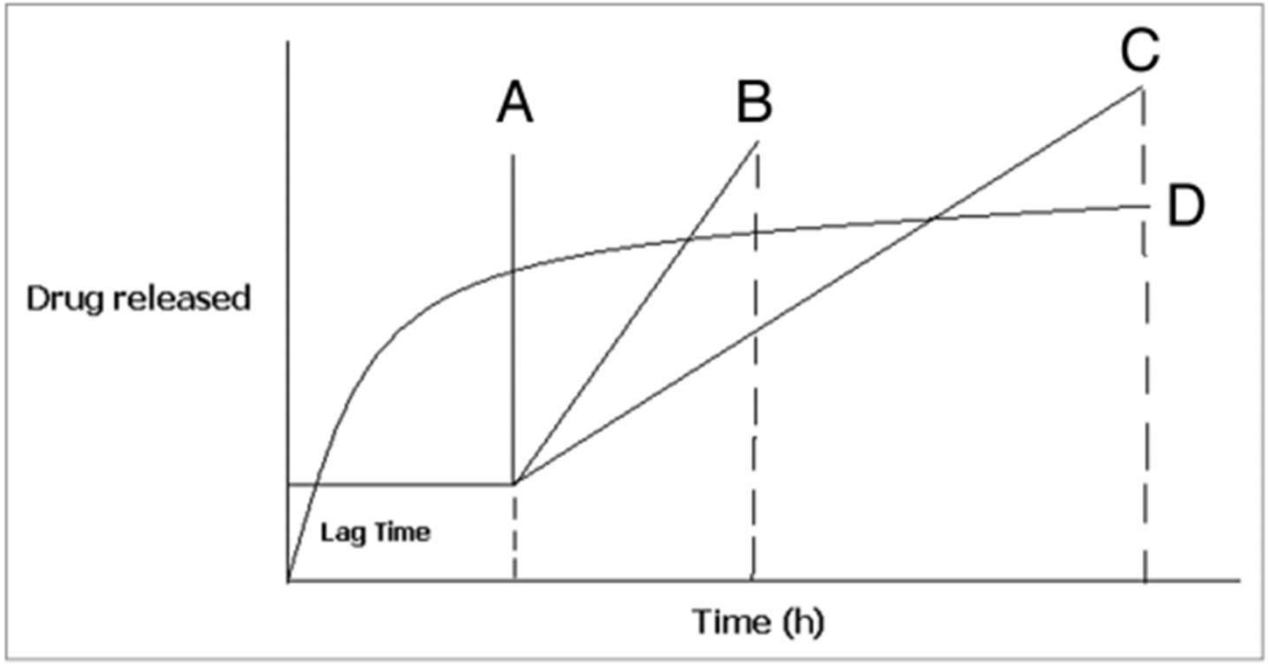


Figure 1. Schematic representation of different drug delivery systems, with (A) sigmoidal release after lag time, (B) delayed release after lag time, (C) sustained release after lag time and (D) extended release without lag time.

Differences between sustained release and controlled release

SUSTAINED RELEASE	CONTROLLED RELEASE
Provide long-term treatment	Provide a constant drug concentration in the blood / tissue.
do not release drug by zero order kinetics Generally drug release is close to first-order kinetics,	Zero order release kinetic Drug release rate and time can be adjusted
Generally do not contain mechanisms leading drug targetting to the site of action	They enable the localization of the active agent in the site of action.