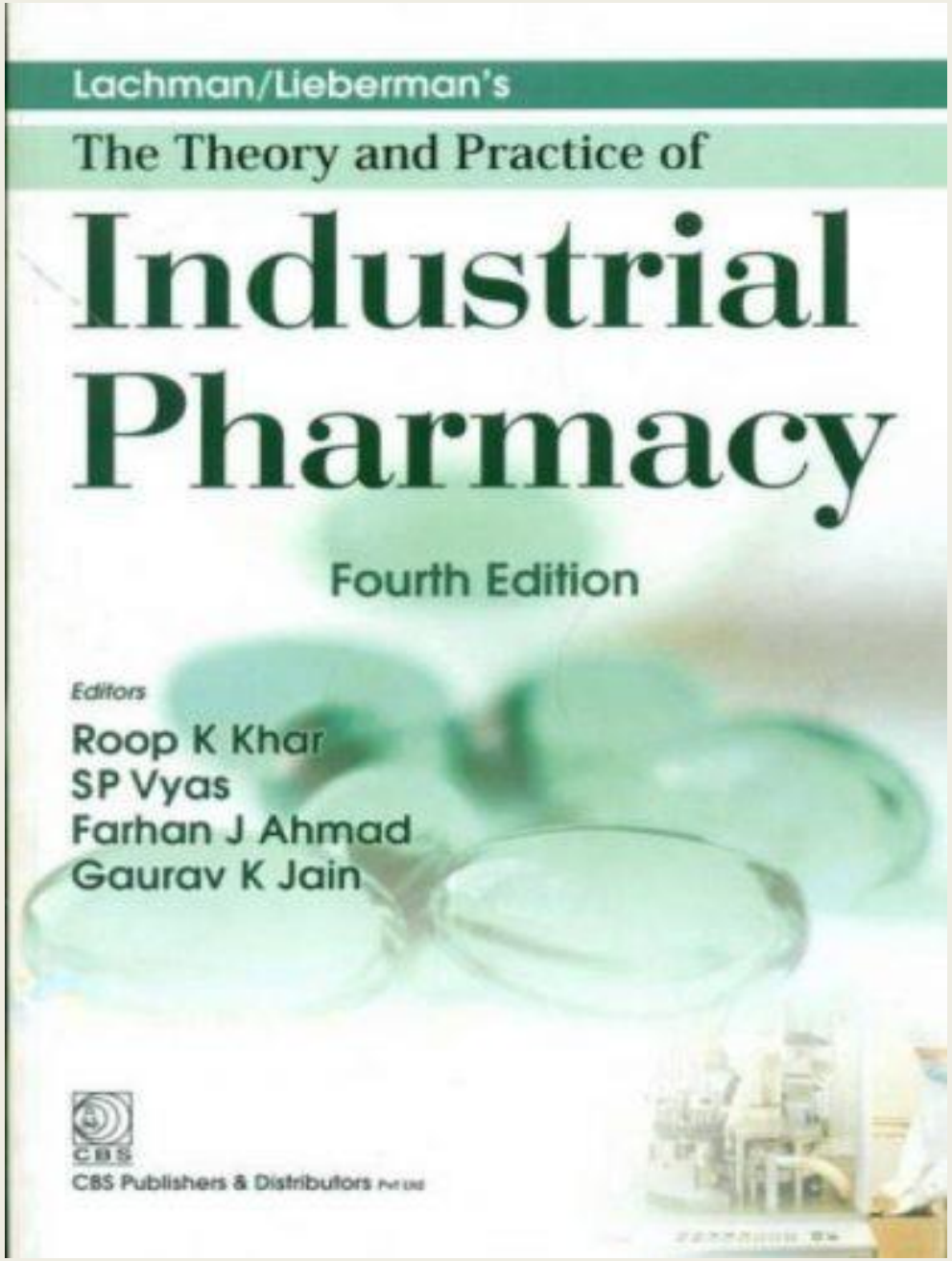
Textbook:

The Theory and Practice of Industrial Pharmacy By Lachman/Lieberman's

4th Edition



Industrial Pharmacy II Syllabus:

Pharmaceutical Dosage Forms:

- Tablets
- Tablet Coating
- Capsules (HGC & SGC)
- Microencapsulation
- Semisolids
- Aerosols

Tablets (oral route)

- **Role in therapy:** for systemic effects
- **Oral route of drug administration (most important method to give systemic effect)**, at least 90% of all drugs used to produce systemic effects are administered by the oral route in comparison with other routes such as parenteral and **Transdermal routes.**

✓ **Drugs that are delivered to body for systemic effects by other routes for examples:**

Insulin = parenteral route, whereas

Nitroglycerin and scopolamine (patches) **Transdermal**

- **Transdermal route** is limited *in its ability to allow effective drug absorption for systemic drug action.*

- **The parenteral route** of administration is **important in treating medical emergencies** in which a subject is *comatose or cannot swallow*, and in providing various types of maintenance therapy for hospitalized patients.

SOLID DOSAGE FORMS

Solid dosage forms represent the preferred class of product because:

1. **Tablets and capsules** are **unit dosage forms** in which *one usual dose of the drug has been accurately placed*.

2. **By comparison**, **liquid oral dosage forms**, such as syrups, suspensions, emulsions, solutions, and elixirs, are usually designed to contain one dose of medication in 5 to 30 ml. The measure of dose performed using a teaspoonful or tablespoonful.

a) Such dose measurement are **error by a factor ranging from 20 to 50%** when drug is self-administered by the patient.

b) **More expensive to ship** (one liquid dosage weight 5 g or more versus 0.25 to 0.4 g for the average tablet).

c) **Breakage or leakage during shipment.**

d) **Taste masking of the drug** in solution even partially.

e) **Less portable and require much more space per number of doses** on the pharmacist's shelf.

f) **Drug are in general less stable (both chemically and physically)** in liquid form than in a dry state and expiration dates tend to be shorter.

REASONS OF HAVING LIQUID DOSAGE FORMS OF A DRUG

1. The liquid form is public for certain types of product (e.g., cough medicines)

2. The product is more effective in a liquid form (e.g., many adsorbents and antacids).

3. The drug(s) are used fairly commonly by young children or elderly, who have trouble swallowing the solid oral dosage forms.

ADVANTAGES TABLETS VS. CAPSULES

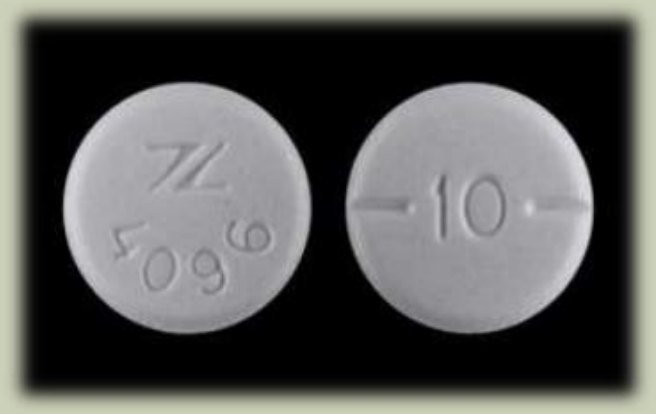
The tablet has a number of advantages over capsules:

1. One major significant advantage, is that the tablet is an essentially **tamperproof dosage form** (any adulteration of a tablet after its manufacture is almost certain to be observed).

- The major advantage of capsules-their ability to hide their contents from sight and to mask or hide the taste or odor of their contents-makes them the most vulnerable to tampering of all dosage forms.

2. **Addition of any liquid to a tablet would produce disintegration if the liquid is aqueous, or would produce visible changes if the liquid is nonaqueous.**

3. **Addition of extraneous powder to a tablet is not readily feasible.**



CONTINUE TABLETS VS. CAPSULES

A major disadvantage of capsules over tablets is their higher cost:

1. Capsules (hard gelatin or soft elastic), employ a capsule shell to contain the drug contents **(The cost of this shell is several tenths of a cent or more, depending on whether the capsule is banded, printed with identification, or otherwise treated)**.

2. In addition to the **cost of filling which is higher** than the typical total cost of tablet production.

ADVANTAGES OF TABLETS

1. A unit dose form, that offer greatest capabilities of all oral dosage forms (O.D.F.) for the **greatest dose precision and the least content variability.**

2. **Their cost is lowest of all O.D.F.**

3. **Lightest and most compact of all O.D.F.**

4. **Easiest and cheapest to package and ship of all O.D.F.**

5. **Product identification is the simplest and cheapest**, requiring no additional processing steps when employing an embossed or monogrammed punch face.

6. **Ease of swallowing with the least tendency for "hang-up" above the stomach**, especially when coated, provided that tablet disintegration is not excessively rapid.

7. **Lend themselves to certain special-release profile products**, such as enteric or delayed-release products.

8. **Better suited to large-scale production than other unit oral forms.**

9. **Best combined properties of chemical, mechanical and microbiologic stability of all the oral forms.**

DISADVANTAGES

- Some drugs resist compression into dense compacts, owing to their amorphous nature or flocculent, low-density character.
- Drugs with poor wetting, slow dissolution properties, intermediate to large dosages, optimum absorption high in the gastrointestinal tract, or any combination of these features may be difficult or impossible to formulate and manufacture as a tablet that will still provide adequate or full drug bioavailability.
- Bitter-tasting drugs, drugs with an objectionable odor, or drugs that are sensitive to oxygen or atmospheric moisture may require encapsulation or entrapment prior to compression (if feasible or practical), or the tablets may require coating. In such cases, the capsule may offer the best and lowest cost approach.

In summary of the foregoing advantages and disadvantages of tablets in comparison to other oral dosage forms, tablets do provide advantages

To the pharmacist:

- Minimal storage space requirements
- Ease of dispensing
- Possibly control

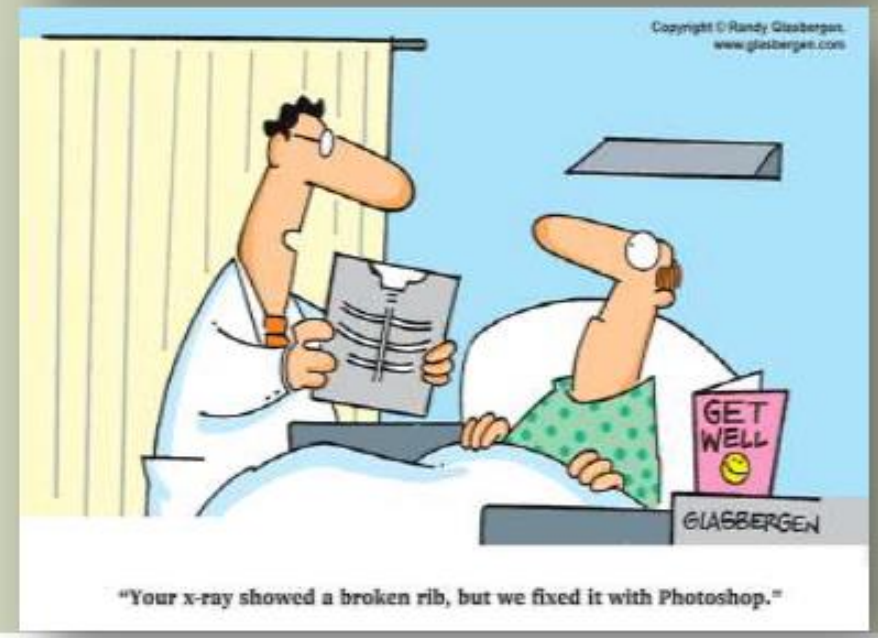
To the patient:

- Convenience of use
- Optimum portability
- Lowest cost

To the physician:

- Flexibility of dosage (with bisected tablets)
- Accuracy
- Precision of dosage in general.

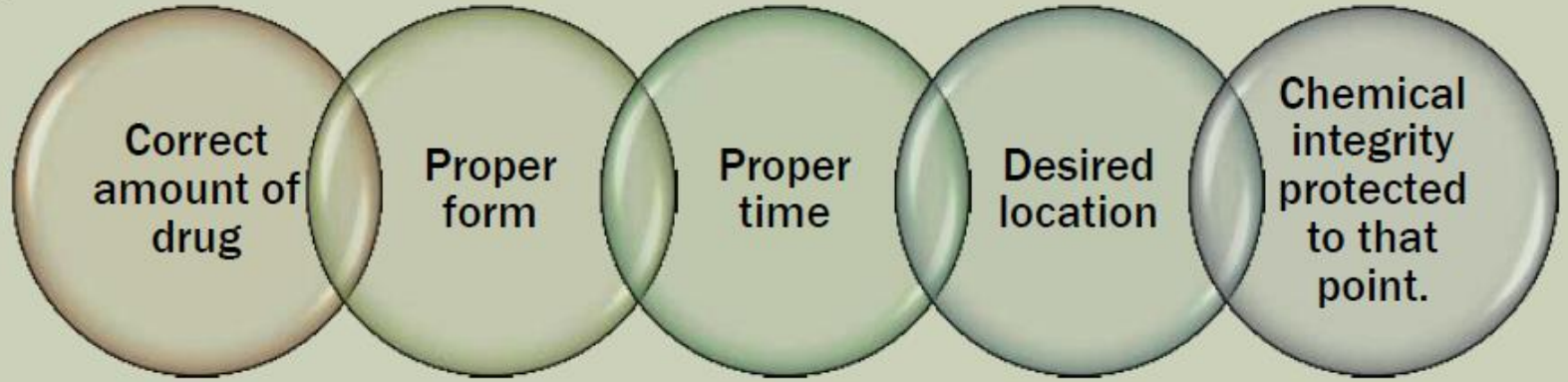
"Each capsule contains your medication, plus a treatment for each of its side effects."



"Your x-ray showed a broken rib, but we fixed it with Photoshop."

PROPERTIES OF IDEAL TABLET

The objective of the design and manufacture of the compressed tablet is to deliver:



Improving efficacy of the drug being formulated into a tablet through:

A tablet:

(1) **Should be an elegant product having its own identity** while being free of defects such as chips, cracks, discoloration, contamination.

(2) **Should have the strength to withstand the rigors of mechanical shocks** encountered in its production, packaging, shipping, and dispensing

(3) **Should have the chemical and physical stability** to maintain its physical attributes over time.

(4) **Must be able to release the medicinal agent(s) in the body in a predictable and reproducible manner.**

(5) **Must have a suitable chemical stability over time** so as not to allow alteration of the medicinal agent(s).

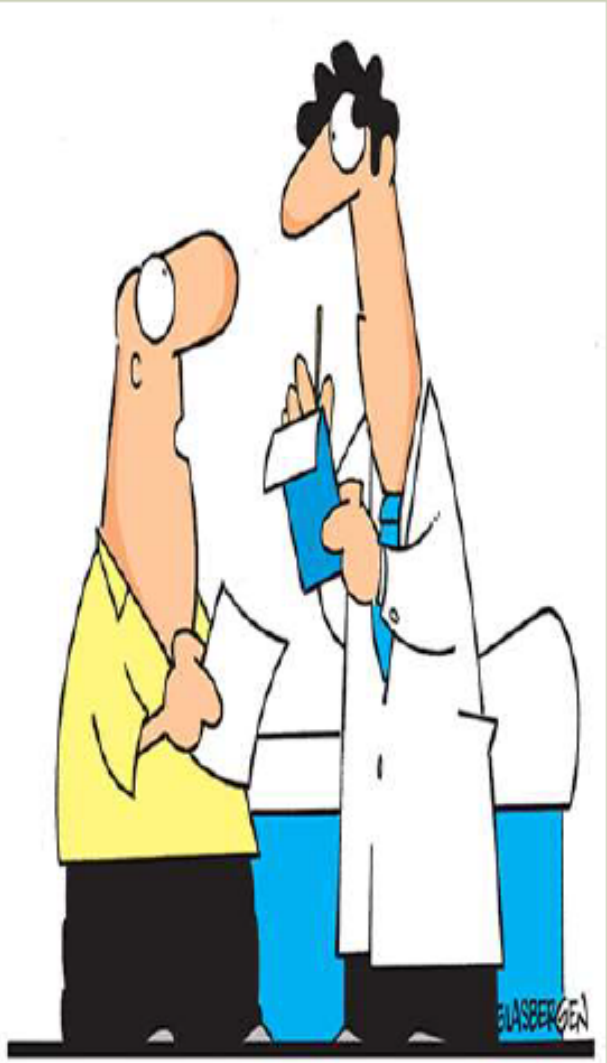
Note:

The physical stability of tablet effects on bioavailability, How?

A. **The design of a tablet that emphasizes only the desired medicinal effects may produce a physically inadequate product.**

B. **The design of a tablet emphasizing only the physical aspects may produce tablets of limited and varying therapeutic effects.**

Ex: 14 nitrofurantoin products, all of which passed the compendial physical requirements, but showed significant bioavailability differences.



"Right now I take a blue pill, a purple pill, an orange pill, a white pill, and a yellow pill. I need you to prescribe a green pill to complete my collection."

Types and classes of tablets

Tablets are classified by:

- Route of administration or function
- Type of drug delivery system they represent within that route
- Form and method of manufacture.

TABLETS INGESTED ORALLY

Note: 90% of the tablets manufactured today are ingested orally and are designed to be swallowed intact, with the exception of chewable tablets.

Compressed tablets or standard compressed tablets

Standard uncoated tablets made by compression

Methods of manufacture: wet granulation, double compaction, or direct compression.

Properties:

1- Provide rapid disintegration and drug release.

2- Exert a local effect in the gastrointestinal tract **(Ex: water-insoluble drugs as the antacids and adsorbents).**

3- Exert a systemic effect in GIT

Drugs that have some aqueous solubility, dissolve from the tablet and disintegrated tablet fragments in GI contents, and are then absorbed and distributed in the body.

Notes: The proper disintegration of the tablet and deaggregation of the tablet fragments are often critical to the proper performance of the dosage form.

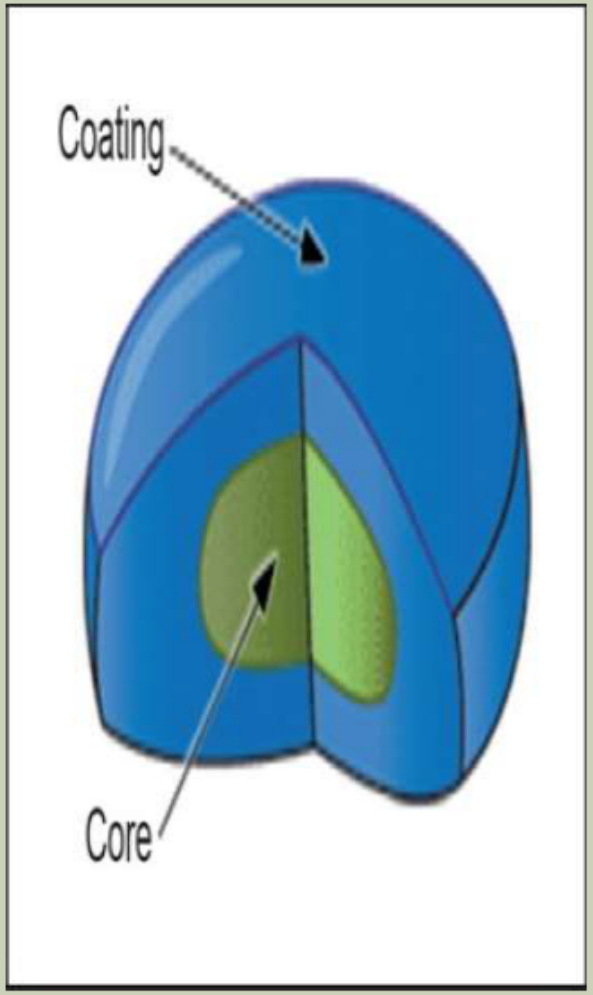
1- The locally acting drugs perform in accordance with their state of deaggregation, since adsorbents and antacids both involve surface activity that increases as their surface area increases.

2- Dissolution is also a surface-related phenomenon, with dissolution rates increasing as a drug's surface area is increased. Thus, tablet breakup and particle deaggregation is also important for drugs to produce systemic effects.

MULTIPLE COMPRESSED TABLETS.

There are two classes of multiple compressed tablets:

1. **Layered tablets**
2. **Compression-coated tablets.**



Important Notes:

i. Both types may be either two-component or three-component systems: two-layer tablet (tablet within a tablet) or three-layer tablets (tablet within a tablet within a tablet).

ii. Both types of tablets usually undergo a light compression as each component is laid down, with the main compression being the final one.

iii. Tablet machine production speeds for multiple compressed tablets are appreciably slower than for standard compressed tablets, especially in the case of compression-coated tablets.

THE LAYERED TABLET

Reasons for preparing such type of tablets in this category:

1. Separate physically or chemically incompatible ingredients
2. Produce repeat-action or prolonged-action products.

- One layer of the layered tablet or the outer tablet of the compression-coated tablet provides the initial dose, rapidly disintegrating in the stomach.

- The other layer or the inner tablet is formulated with components that are insoluble in gastric media but released in the intestinal environment.

Its performance is highly dependent on gastric emptying.

If the second layer or core tablet quickly leaves the stomach following release of the initial fast-release dose, an entirely different blood level profile results than if there is a several-hour or longer delay before the second fraction is emptied.

REPEATED-ACTION TABLETS

Types: multiple compressed tablets and sugar-coated tablets

The mode of operation and limitations based on: uncontrolled and unpredictable gastric emptying.

1. **The core tablet is usually coated with shellac or an enteric polymer** so that it will not release its drug load in the stomach.
2. **The second dose of the drug is then added in the sugar coating**, either in solution in the sugar syrup or as a part of the dusting powder added for rapid coat buildup.

DELAYED-ACTION AND ENTERIC COATED TABLETS

Intended to release a drug after some time delay or after the tablet has passed through one part of the GIT into another. The enteric coated tablet is the most common example of a delayed-action tablet product.

Important notes: **1- All enteric coated tablet (remain intact in the stomach but quickly release in the upper intestine) are a type of delayed-action tablet.**

2- Not all delayed-action tablets are enteric or are intended to produce the enteric effect.

Coat: The coatings to produce enteric effects are primarily mixed acid functionality and acid ester functionality synthetic or modified natural polymers.

Ex: Cellulose acetate phthalate (CAP), polyvinyl acetate phthalate (PVAP) and hydroxypropyl methylcellulose phthalate (HPMCP).

Properties of enteric coat polymers:

These polymers, being acid esters, are insoluble in gastric media that have a pH of up to about 4; they are intended to hydrate and begin dissolving as the tablets leave the stomach, enter the duodenum (pH of 4 to 6), and move further along the small intestine, where the pH increases to a range of 7 to 8.

Mechanism of polymers:

i. These polymer lose their film integrity, thereby admitting intestinal fluid and releasing drug, where ionisation of the residual carboxyl groups on the chain and subsequent hydration.

ii. The presence of esterases in the intestinal fluid that break down ester linkages of the polymer chains may also play some role, as may surface activity effects of bile salts and other components in the bile that enter the upper small intestine via the bile duct.

Enteric coatings are employed for a number of therapeutic, safety, and medicinal reasons:

1. One method of reducing or eliminating the irritation from such drugs. (example: Some drug are irritating when directly exposed to the gastric mucosa, including aspirin and strong electrolytes such as NH_4Cl).
2. To get rid of some drugs effect especially if they release in the stomach they may produce nausea and vomiting.
3. Necessary to bring the drug through stomach to the more neutral intestinal contents as the low pH of the stomach destroys other drugs (for example, erythromycin).
4. Desire to release the drug undiluted and in highest concentration possible within the intestine. (examples are intestinal antibacterial or antiseptic agents)

Reference: The Theory and Practice of Industrial Pharmacy
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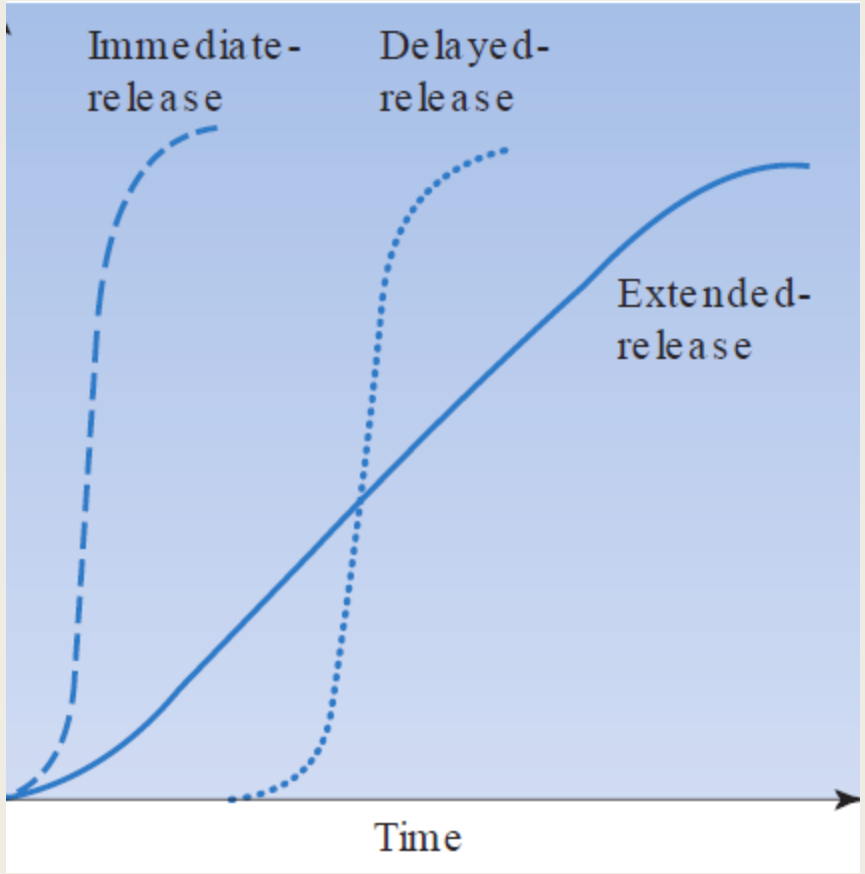
Modified Release Products:

1- Delayed release (enteric coated)

2- Extended Release (ER)

Extended Release (ER) dosage forms: are designed to release their medication in a controlled manner, at predetermined rate, duration and location to achieve and maintain optimum therapeutic blood levels of drug. They allow a reduction of dosing frequency from that necessitated by an immediate release dosage form. The release of drug form these dosage forms is over an extended period of 12-24 hours.



Sustained release (SR), sustained action (SA), prolonged action (PA), controlled release (CR), extended release (ER), timed release (TR) and long acting (LA).

Rapidly disintegrating or dissolving tablets

Are characterised by disintegrating or dissolving in the mouth within 1 min. and some within 10 seconds. E.g. Clarinex Reditabs. Tablets of this type are designed for children and the elderly who have difficulty in swallowing tablets. They liquefy on the tongue and the patient swallows the liquid.