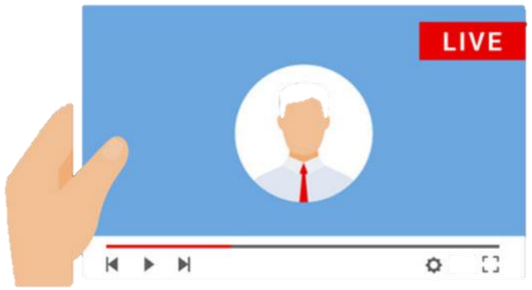


Welcome to "Live online class"

Tablets

Solid Dosage forms

- Solid-dosage forms broadly encompass two types of formulation: **Tablets and capsules**
- It has been estimated that solid-dosage forms **90% of all dosage** forms
- Most important dosage forms in the treatment and management of disease states
- The widespread use → their **convenience** and also the **diversity of tablet** types

Tablets: Advantages

- Tablets are **tamperproof** dosage formulation
- Unit dose with **greatest dose precision** and the **least content variability**
- Greatest **ease of swallowing**
- Certain **special-release profile products**, such as enteric or delayed-release products
- **Lowest Cost and Optimum Portability**
- Light and most compact
- Easiest and cheapest to package, store and ship
- Product identification is simplest and cheapest (no additional processing steps)
- Better suited to **large-scale production**
- **Combined properties of chemical, mechanical and microbiologic stability**

Tablets: Disadvantages

- Manufacture of tablets requires a **series of unit operations** → Increased level of product loss at each stage in the manufacturing process
- The absorption of tablets is **dependent on physiological factors** → Shows inter-patient variation
- **Compression properties** of certain drugs are poor (amorphous, flocculent, low-density) → Problems in formulation and manufacture as tablets
- **Administration** of tablets to **children, elderly and sick** → Problematic
- Drugs with poor wetting, slow dissolution properties, intermediate to large dosages, optimum absorption high in the GIT are difficult to formulate → **Drug bioavailability issues**
- Bitter-tasting drugs, drugs with an objectionable odor, or drugs that are sensitive to oxygen or atmospheric moisture → **Require encapsulation or entrapment** prior to compression or the tablets may require coating

Tablets: Design and formulation

1. Diluents/fillers/bulking agents
2. Binders & adhesives (granulators)
3. Disintegrants
4. Lubricants, Antiadherent & Glidant
5. Colors, flavors & sweeteners

Tablets: Diluents/fillers/Bulking agents (1)

- **Diluents/fillers designed to make up the required bulk of the tablet when the drug dosage Itself is inadequate to produce this bulk**
- The dose of some drugs is sufficiently high that no filler is required
- Round tablets for ingestion are usually in a size range of **3/16 to 1/2 inch (120-700mg)**

  [Oval tablets are big 800 mg or more]
- Tablet formulations may contain a diluent for secondary reasons: to provide better tablet properties such as
  - **improved cohesion,**
  - **to permit the use of direct compression manufacturing**
  - **to promote the flow**

Tablets: Diluents/fillers/Bulking agents (2)

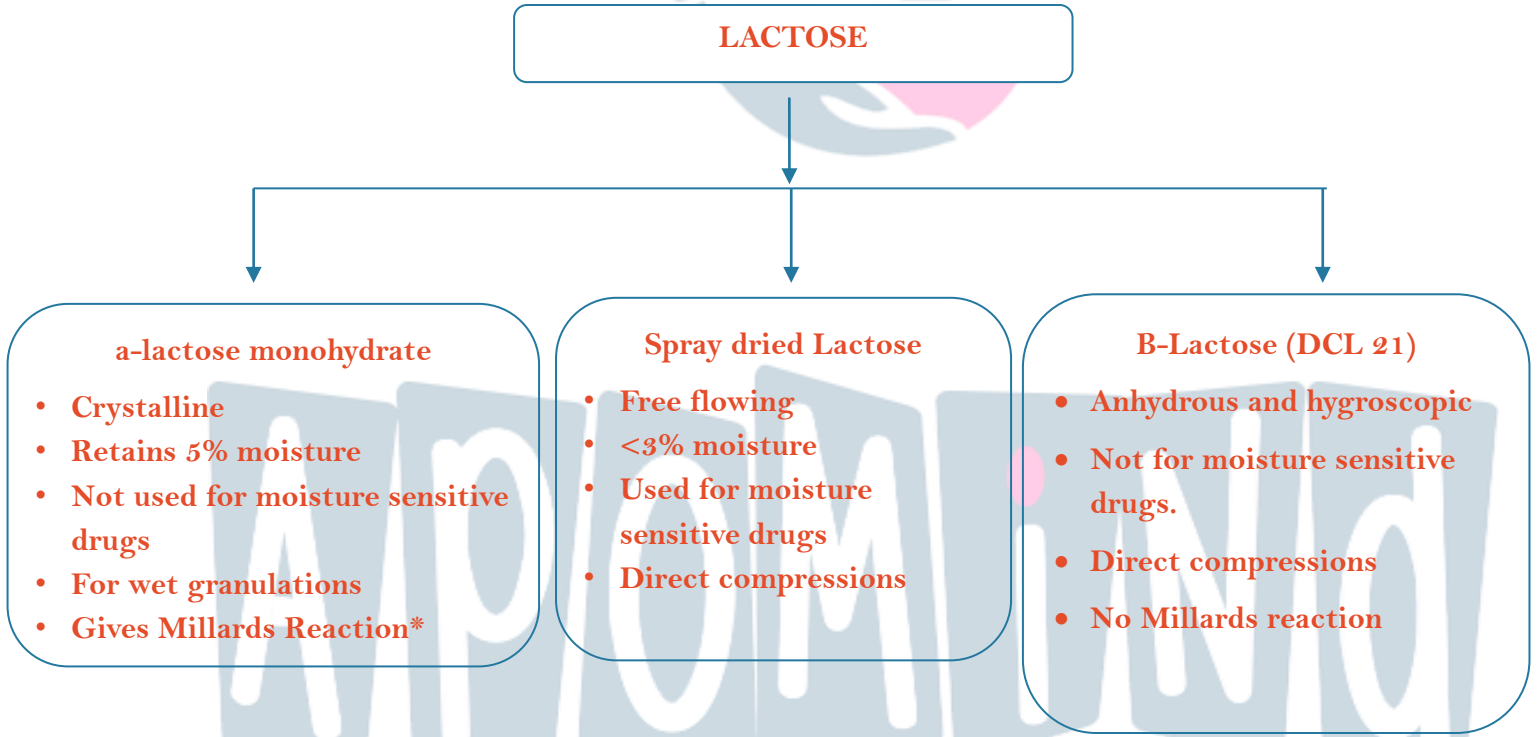
IDEAL PROPERTIES OF DILUENTS

- Nontoxic and acceptable to the regulatory agencies
- Low cost
- **They must not be contraindicated by themselves (e.g., sucrose) or because of a component (e.g., sodium) in any segment of the population**
- Physiologically inert
- **Stable : Physically/Chemically/Microbiologically**
- No deleterious effect on the bioavailability of the drug(s) in the product

Tablets: Diluents/fillers/Bulking agents (3)

LACTOSE

- Lactose is **most widely** used diluents in tablets
- Lactose is water soluble diluent, used for the immediate release of the drug



Millard's Reaction*(Physical Incompatibility):-- Hydrous lactose + ½ Amine containing drug forms darkening of tablet or browning due to formation of furfuraldehyde

Tablets: Diluents/fillers/Bulking agents (4)

Starch and dextrose

Starch

- Starch may come from corn, wheat, and potato and may ***give rise to soft tablets***
- Moisture content: ***11-14%***
- **Star- Rx – 1500**
  - Free flowing, directly compressible starch
  - Used as diluents, binder, disintegrating agent, self-lubricating, and Glidant (0.25%)
  - Moisture content: ***10% (Never use with Magnesium stearate [>0.5%])***
- **Emdex & Celutab (contains 90-92% dextrose, 3-5% maltose)**
  - Hydrolyzed starches which are free flowing and directly compressible
  - Sweet in taste and can be used in replace of Mannitol (Chewable tablets)

Dextrose (Cerelose®):

- ***Replace the lactose to reduce the tablet to darken***

Tablets: Diluents/fillers/Bulking agents (5)

MANNITOL AND SORBITOL

- **Mannitol (Pearlitol®):--**
  - Most Expensive
  - Used mainly in the chewable tablets: **Negative heat of salvation, slow solubility and pleasant feeling in mouth**
  - It is *non-hygroscopic , hence, used in moisture sensitive vitamin formulation*
  - Poor flow **(Require high amounts of lubricants)**
  - **Non reducing sugar (No Millard's reaction).**
- **Sorbitol:--**
  - It is **optical isomer of Mannitol** but is hygroscopic (**above 65% moisture**)
  - It has **low caloric content and non-carcinogenic**.

Tablets: Diluents/fillers/Bulking agents (6)

SUCROSE

- **SUCROSE**
  - DiPac® → 97% Sucrose + 3% modified dextrin
  - Sugartab → 90-93% sucrose + 7-10% invert sugar
  - NuTab® → 95% sucrose + 4% invert sugar with small amount of corn starch & magnesium stearate

Tablets: Diluents/fillers/Bulking agents (7)

Micro Crystalline Cellulose – MCC

- Good flowability
- ***Direct compressible***
- Used as **disintegrating agent**
- Problems of capping and lamination
- Water insoluble, hygroscopic and on storage becomes soft

Avicel 101(Powder - PH 101)

- For direct compression and wet granulation method

Avicel 102(Granules – PH 102)

- It have large particles size and better flowability

Avicel 103, 112, 113

- Reduced moisture content and ideal for moisture sensitive materials

Tablets: Diluents/fillers/Bulking agents (8)

Calcium Salts

- Also known as **Emcompress®, Ditab®, and Fujicalin®**
- DCP (Dibasic calcium phosphate), calcium sulfate and TCP contain water of crystallization → low affinity for atmospheric moisture → Hence, used for water sensitive drugs → It shows hardening effect
- DCP is virtually insoluble in water and hence used in conjunction with disintegrating agent
- It also shows fragmentation tendency
- **Calcium based diluents can cause interaction with tetracycline's API because it from insoluble complex and salts, which reduces absorption and bioavailability**
- **Black particles on friction**

Tablets: Binders & Adhesives (Granulators) (1)

- They ***imparts cohesive properties*** to powdered material to form granules for tableting.
- Binders more active as a solution form than solid form
- More the binder used, harder is the tablet formed
- Natural Gums
  - **Acacia & Tragacanth** (10-25%) -- They are of natural origin so variable in composition easily attacked by microorganism → Use equipment with temperature >37°C
- **Gelatin** (10-20%):-- Natural protein (Easier to prepare solution than natural gums)
- **Starch paste** (5-20%):--
  - Prepared by dispersing starch into water when heated
  - The paste must be translucent rather than clear
  - On heating starch hydrolyzed to ***dextrin & glucose*** → While clear paste indicates complete conversion to glucose

Tablets: Binders & Adhesives (Granulators) (2)

- **Liquid glucose (50-74%)**
  - For wet granulation
  - Produces hard and brittle tablets
- **Modified Natural polymers**
  - ***Alginates and cellulose derive***: -- Methyl cellulose, Hydroxy propyl methyl cellulose **(HPMC)**, Hydroxy propyl cellulose **(HPC)** [for both alcoholic & aqueous solution]
    - For direct compression & their aqueous solution is adhesive
  - ***Ethyl Cellulose***: -- It is used only with solution alcoholic & it can retard the disintegration & dissolution of drugs
- **Polyvinyl pyrrolidone (PVP) (2-10%) - Grades K30 or K90**
  - Synthetic polymer
  - Adhesive in either aqueous or alcoholic solution

Tablets: Disintegrant (1)

- It **counteracts the cohesive action** due to applied compression forces and binders
- Although most of the tablets contains disinter grants, certain exceptions are:--
  - *Buccal Tablets*
  - *Sustained Release tablets*
  - *Lozenges*
  - *Implants*
  - *Chewable Tablets*
- Disintegration agents may act by either 4 mechanism:--
  - ***Swell and atlast burst***
  - ***By chemical reaction producing effervescence***
  - ***Enzymatic action***
  - ***By wetting action***

Tablets: Disintegrant (2)

1. **Swell and atlast burst:--**

Eg:--

- Starch USP(5-20%):-- Most commonly used
- Modified starch(1-8%) :-- Primogel® and Explotab® are low substituted carboxy methyl starches
- Clays → Bentonite or Veegum (10%) : give off white appearance.
- Cross linked sodium CMC(1-5%):--Ac-di-sol® , Crosscarmelose®
- Cross linked polyvinyl pyrrolidone: -- These are called **super disintegrants**. E.g. Sodium starch gluconate (SSG), croscarmellose sodium (CCS), crospovidone.
- Ion exchange resins: -- Iodion 414® or palacrillin K+ → it is a cation exchange resin.

- **Starch swells in all 3 dimensions whereas cellulose swells in 2 dimensions only**

Tablets: LUBRICANTS

- They are intended to ***reduce the friction during tablet ejection between walls of the tablet*** and walls of the die cavity in which tablet was formed
- Lubricants based ***upon fatty acids*** are insoluble in water & ***hence can retard the disintegration & dissolution time***
- **Water soluble lubricants**: PEG 6000, [Macrogol 6000 or Carbowax], Magnesium Lauryl Sulfate, Fumaric acid enhances dissolution of hydrophobic granules
- **Talc (5%):**-- Both **Glidant + lubricant activity** *(Contains Iron, so carefully used if any formula contains drug which breakdown is catalysed by Fe^{2+})*

Tablets: ANTIADHERANTS & GLIDANTS

Antiadherent

- *They are used to reduce the sticking & adhesion of any of tablet granulation/powder to the punches of die wall*
- Eg: -- **Starch and its derivatives, Talc, Mg-stearate, and colloidal Silica**

Glidant (Flow promoters):--

- They are intended to *promote flow of the tablet granules from hoper & reducing the friction between the particles*
- E.g. **colloidal silicon dioxide [Aerosil, Cab-O-Sil, Syloid]; Calcium & Magnesium Stearates → 0.25 – 1%, Corn Starch (5-10%)**

Tablets: COLORS

Purpose ---

- *Disguising of color drugs;*
- *Product identification;*
- *Production of more elegant product.*

Two forms of color are used in tablets: -- **FD&C dyes and D&C dyes** *(applied as an solution in granulation process or as lakes)*

Lakes

- *They are dyes that has been absorbed on hydrous oxide and usually employed as dry powders for coloring. They contain 10-30% of pure dye & maximum upto 50%*

Tablets: FLAVORS

- Used mostly in **chewable tablets** or that are intended to use in mouth
- **Water soluble flavor have less stability**
- Flavored oils added to tablets granulations in solvent -- dispersed on dyes and other absorbents or emulsified in aqueous granulating agent
- Maximum amount of oils added upto **0.5-0.75%**

Tablets: SWEETENERS

- Only used in chewable tablets and mouth dissolving tablets
- **Mannitol is 72%** sweet as sucrose but expensive
- **Saccharin (Artificial Sugar):-- 500 times sweeter** than sucrose but it is **carcinogenic** in nature and bitter taste after use
- **Aspartame (dipeptide aspartic acid + Phenylalanine):-- 200 times sweeter** but saccharin but this aspartame **lack stability** in the presence of moisture and it is **hygroscopic**


Failure is success in progress.
Albert Einstein
quotefancy