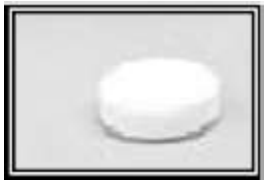
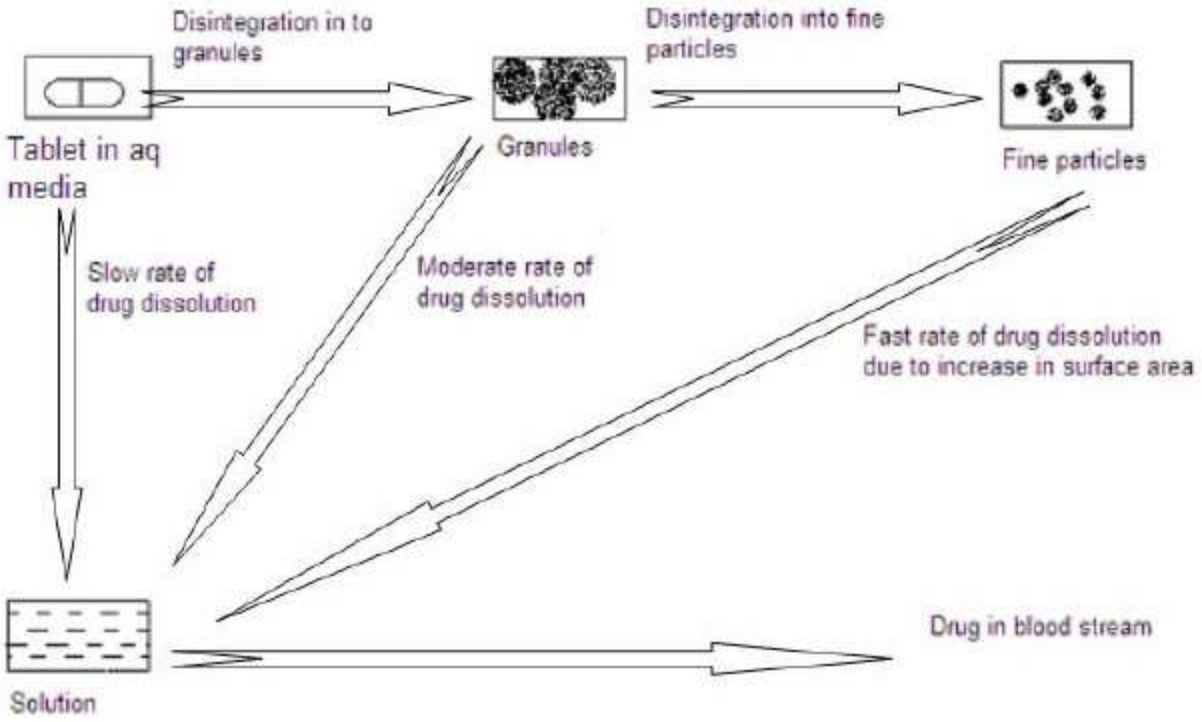
TABLETS

Oral Solid Dosage Forms

Tablets

Is solid pharmaceutical dosage forms containing drug substances with or without suitable diluents and prepared either by compression or molding methods




Disintegration in to granules
Disintegration into fine particles
Tablet in aq media
Granules
Fine particles
Slow rate of drug dissolution
Moderate rate of drug dissolution
Fast rate of drug dissolution due to increase in surface area
Drug in blood stream
Solution

advantages afforded to the manufacturer

1- simplicity

2- economy of preparation

3-stability

4-convenience in packaging, shipping and dispensing

advantages to the patient

1-accuracy of dosage

2- compactness

3-portability

4 blandness of taste

5-ease of administration.

- Tablets may differ greatly in size and weight depending on the amount of drug substance present and the intended method of administration.

- They are divided into two general classes, whether they are made by compression or molding.

- **Compressed Tablets (CT):**

Are formed by compression and contain no **special coating**.

They are made from powdered, crystalline or granular materials, **alone or in combination** with binders, disintegrants, controlled-release polymers, lubricants, diluents and, in many cases, colorants

- **Sugar-Coated Tablets (SCT)** :

These are compressed tablets containing a sugar coating. Such coatings may be colored and are beneficial in covering up drug substances possessing objectionable tastes or odors, and in protecting materials sensitive to oxidation.

- **Film-Coated Tablets (FCT)** :

These are compressed tablets which are covered with a thin layer or film of a water-soluble material. A number of polymeric substances with film-forming properties may be used. Film coating imparts the same general characteristics as sugar coating with the added advantage of a greatly reduced time period required for the coating operation.

- **Enteric-Coated Tablets (ECT)** - These are compressed tablets coated with substances that resist solution in gastric fluid but disintegrate in the intestine. It can be used for tablets containing drug substances which are inactivated or destroyed in the stomach, for those which irritate the mucosa or as a means of delayed release of the medication.

- **Multiple Compressed Tablets (MCT)** :

These are compressed tablets made by more than one compression cycle.

- Layered Tablets - Such tablets are prepared by compressing additional tablet granulation on a previously compressed granulation. The operation may be repeated to produce multilayered tablets of two or three layers. Special tablet presses are required to make layered tablets

- **Press-Coated Tablets - dry-coated,** are prepared by feeding previously compressed tablets into a special tableting machine and compressing another granulation layer around the preformed tablets.

❖ They have all the advantages of **compressed tablets**, i.e, monogramming, speed of disintegration, etc, while retaining the attributes of sugar-coated tablets in masking the taste of the drug substance in the core tablets...

- ❖ Press-coated tablets also can be used to separate incompatible drug substances.
- ❖ In addition, they can provide a means to give an enteric coating to the core tablets.
- **Both types of multiple-compressed tablets have been used widely in the design of prolonged-action dosage forms.**

- **Controlled-Release Tablets** - Compressed tablets can be formulated to release the drug **slowly over a prolonged period of time**. Hence, referred to as Prolonged-Release or Sustained-Release dosage forms as well. These tablets (capsule versions) categorized into three types:

- **(1)** those which respond to some **physiological condition** to release the drug, such as enteric coatings.
- **(2)** those that release the drug in **a relatively steady, controlled manner.**
- **(3**) those that combine **combinations of mechanisms to release "pulses"** of drug, such as repeat-action tablets

- Tablets for Solution:

Compressed tablets to be used for preparing solutions or imparting given characteristics to solutions must be **labeled** to indicate that they are not to be swallowed.

Examples of these tablet:

Potassium Permanganate Tablets for Solution

➢ Effervescent Tablets:

In addition to the drug substance, these contain **sodium bicarbonate** and an **organic acid** such as **tartaric and citric**.

In the presence of water, these additives react liberating **carbon dioxide** which acts as **a distintegrator** and produces effervescence.

Except for small quantities of lubricants present, effervescent tablets are **soluble.**

- **Soluble tablet (dispensing tablet DT):**

Tablets are solids of uniform shape and dimensions, usually circular, with either flat or convex faces, the distance between faces being less than the diameter. Water soluble tablets are intended for adminstration after dissolution in water and contain an active ingredient should be totally soluble in water at used concentrations. All the excipients used to formulate these tablets are required to be completely soluble in water including the glidants, binders, etc. So, manufacturing of this kind of tablets are challenge for the formulator. Companies manufacturing these tablets have patented them.

➢ **Hypodermic Tablets (HT)** :

Hypodermic tablets are **soft, readily soluble** tablets and originally were used for the preparation of solutions to be injected. Since stable parenteral solutions are now available for most drug substances, there is no justification for the use of hypodermic tablets for injection.

➢ ***Molded Tablets [Tablet Triturates (TT)]:***

Tablet triturates are small,usually cylindric molded or compressed tablets. Though rarely used today,they provid an extemporaneous method of preparation by the pharmacist.The drugs employed were quite potent and were mixed with lactose as diluent and powdered acasia as abinder then the mixture was moistened to produce amoldable compactable mass which was forced through amold board mad from wood or plastic then the tablets were ejected and allow to dry.

For preparation of this tablets alcohole was used to moistened(wet) the powder mass**,as alcohole evaporate it leads to drug migration and also formation of soft and friable tablet.**

Other problem arising from compression of these tablets is the failure to find **a lubricant that is completely water soluble,**

that was this type of tablet rarely used today.

- ***Compressed suppositories or insert occasionally vaginal suppositories such as Metronidazole tablets which are prepared by compression***.

Tablets for this use usually contain **lactose** as the diluent. In this case, as well as for any tablet intended for administration other than by swallowing, the label must indicate the manner in which it is to be used.

- **Buccal Tablets:**

These are **small, flat, oval tablets**.

Tablets intended for buccal administration by inserting into the buccal pouch may dissolve slowly; therefore, they are formulated and compressed with sufficient pressure to give a hard tablet.

- **Some newer approaches use tablets that melt at body temperatures.**

The matrix of the tablet is solidified while the drug is in solution. After melting, the drug is automatically in solution and available for absorption, **thus eliminating dissolution as a rate-limiting step in the absorption of poorly soluble compounds.**

- **Sublingual tablets:**

* As those containing **nitroglycerin, isoproterenol hydrochloride**, are placed under the tongue.

Sublingual tablets **dissolve rapidly** and the drug substances are absorbed readily by this form of administration.

Chewable tablet

The patients who have difficulty in swallowing tablets whole or for children who have not yet learnt to swallow a tablet , chewable tablet serves as an **attractive alternative**. The added advantage of this medication is that it can be taken at any time or when water is not available.
Mannitol is normally used as a base due to **low hygroscopy and more importantly, it gives pleasant**, **cooling sensation**.

Antacid tablets are invariably prepared as chewable to obtain quick ingestion relief as well as the antacid dose is too large to swallow and the activity is related to particle size.

Another example is multivitamin tablet which a patient can take as a daily dose.

THANK YOU

TABLETS

Processing excipients
Lecture 5 & 6

➢ Compressed Tablets (CT)

In order for medicinal substances, with or without diluents, to be made into solid dosage forms with pressure, using available equipment, it is necessary that the material, either in crystalline or powdered form, possess a number of physical characteristics. These characteristics include the ability to flow freely, cohesiveness and lubrication

- **After compression, the tablets must have a number of additional attributes such as**

1. appearance,

2. hardness,

3. disintegration ability,

4. appropriate dissolution characteristics and

5. uniformity which also are influenced both by :

- **the method of preparation and by**
- **the added materials present in the formulation.**

➢ Tablet Ingredients

In addition to the active or therapeutic ingredient, tablets contain a number of inert materials(excipients). They are classified according to the part they play in the finished tablet.

1- those which help to impart satisfactory processing and compression characteristics to the formulation (diluents, binders, glidants and lubricants).

2. The second group of added substances helps to give additional desirable physical characteristics to the finished tablet (disintegrants, colors, and in the case of chewable tablets, flavors and sweetening agents, and in the case of controlled- release tablets, polymers or waxes or other solubility-retarding materials)

Diluents

- Are filler designed to increase the bulk when the dosage of drug is inadequate to produce this bulk.The dose of some drug is sufficiently high that no diluent is needed like aspirin and antibiotics . Tablet weight range between 120 -700mg (round)and up to 800 mg in case of oval tablet because more easily to be swallowed.
- Diluents used for this purpose include dicalcium phosphate, calcium sulfate, lactose, cellulose, kaolin, mannitol, sodium chloride, dry starch and powdered sugar.

- Certain diluents, such as mannitol, lactose, sorbitol, sucrose, when present in sufficient quantity, can impart properties to some compressed tablets that permit disintegration in the mouth by chewing.
- Diluents used as excipients for direct compression formulas have been subjected to prior processing to give them flowability and compressibility.

Selection of the diluent

Is based partly on the:

1. **experience of the manufacturer**
2. **on diluent cost**
3. **compatibility with other tablet ingredients .**

- **However, in the formulation of new therapeutic agents, the compatibility of the diluents with the drug must be considered, e.g:**
- **calcium salts used as diluents for the broad-spectrum antibiotic tetracycline have been shown to interfere with the drug's absorption from the gastrointestinal tract(due to the formation of non absorbable complex).**
- **When drug substances have low water solubility, it is recommended that water-soluble diluents be used to avoid possible bioavailability problems.**

- Highly adsorbent substances, e.g, bentonite and kaolin, are to be avoided in making tablets of drugs used clinically in small dosage, such as the cardiac glycosides, alkaloids and the synthetic estrogens WHY??.Because these drug substances may be adsorbed after administration.

- The combination of amine bases with lactose, or amine salts with lactose in the presence of an alkaline lubricant, results in tablets which discolor on aging.

- Microcrystalline cellulose (Avicel) usually is used as an excipient in direct-compression formulas. However, its presence in **5-15%** concentrations in wet granulations has been shown to be beneficial in the granulation and drying processes in minimizing core-hardening of the tablets and in reducing tablet mottling.
- Dextrose **Cerelose** comes in two form hydrous and anhydrous and used combined to replace spray dried lactose to reduce the darken tendency of tablet.
- Mannitol is the most expensive diluent . It is non hygroscopic and can be used in vitamin formulation.it have pleasant feel in mouth so they are used in chewable tablet.
- Sorbitol is an optical isomer of mannitol and sometimes combined in mannitol formulation to reduce the cost. Both mannitol and sorbitol have low coloric content and are non carcinogenic.
- Many ingredients are used for several different purposes, even within the same formulation; e.g, **corn starch** can be used in **paste form** as binder, in **dry form** as disintegrant.

Binder

- **Binder** define as agents used to impart cohesive qualities to the powdered material to insures the tablet remaining intact after compression, as well as improving the free- flowing qualities by the formulation of granules of desired hardness and size.

- Commonly used binders include: starch, gelatin and sugars as sucrose, glucose, dextrose, and lactose.

- Natural and synthetic gums which have been used include acacia, sodium alginate, carboxy- methylcellulose, methylcellulose, polyvinyl pyrrolidone, Veegum.
- Other agents which may be considered binders under certain circumstances are **polyethylene glycol, ethylcellulose, waxes, water and alcohol.**

- The quantity of binder used has considerable influence on the characteristics of the compressed tablets.
- The use of too much binder or too strong a binder will make a hard tablet which will not disintegrate easily and which will cause excessive wear of punches and dies.
- Usually materials which have no cohesive qualities of their own will require a stronger binder than those with these qualities.

- Binders are used both as **a solution and in a dry form** depending on other ingredients and method of preparation.

- The same amount of binder in solution will be **more effective** than if it were in a dry form and moistened with the solvent. So it is preferable to incorporate the binding agent in solution.

- If the drug substance is adversely affected by an aqueous binder , a non aqueous binder can be used or binder can be added dry.

- The direct-compression method for preparing tablets requires a material that not only is free-flowing but also sufficiently cohesive to act as a binder.

1. Acacia and tragacanth are employed in solution in range of 10-25% alone or in combination they are more effective in solution form.

Disadvantage :contamination with bacteria ,when used in dry granulation they should be heated above 37°C to reduce microbial growth.Because they are of natural origin, they are variable in composition and performance.

2.Gelatine:natural protein and used some times in combination with the acacia gum,easily to prepare in solution form and form tablet as equally hard as acacia and tragacanth.

3. Starch Paste :most commonly used granulating agent prepared by dispersing starch into water and heated for some prescribed time.

The starch hydrolyzed to dextrin and glucose(a properly made paste is translucent rather than clear which indicate complete conversion to glucose)

4.Liquid glucose 50% solution is used as common wet granulating agent.

5.Sucrose solution 50-74%.

These sugar solution are capable of producing hard tablet but some what brittle compact .they are low cost. Unless the sugar solution are highly concentrated , bacterial proliferation is problem.

6.Modified natural polymer, such as alginate and cellulose derivative (methyl cellulose ,hydroxypropyl methyl cellulose)

Used in direct compression in dry form and the aqueous solution have adhesive properties.HPMC used as alcoholic solution to provide anhydrous condition. Ethyl cellulose alcoholic solution also used to provide retardation to disintegration and dissolution.

Polyvinylpyrroloidine synthetic polymer used as aqueous or alcoholic binding solution. It has some capabilities of dry binder.

Lubricants,anti adherant and glidant

- **Their functions in tablet manufacture are:-**

1. Prevent adhesion of the tablet material to the surface of the dies and punches.
2. Reduce inter particle friction.
3. Facilitate the ejection of the tablets from the die cavity.
4. May improve the rate of flow of the tablet granulation.

- Commonly used lubricants include: talc, magnesium stearate, calcium stearate ,stearic acid, hydrogenated vegetable oils and (PEG).

- **Note:**

Most lubricants, with the exception of talc, are used in concentrations less than **1% ,** when used alone, talc may require concentrations **as high as 5%** ,corn starch at 5-10% .colloidal silica such as Cab-o-Sil,syloid or Aerosil in 0.25-3% concentration.

- Lubricants are in most cases hydrophobic materials. Poor selection or excessive amounts can result in poor tablet disintegration and or delayed dissolution of the drug substance

- **Anti adherants**: reduce sticking and adhesion of the tablet granulation or powder to the faces of the punches or to the die walls.
- **Glidants** promote the flow of the tablet granulation or powder materials by reducing friction among particles.
- Lubricant are intended to reduce the friction during tablet ejection between the wall of tablet and wall of the die.

Since lubrication basically is a coating process, the finer particle size of lubricant, the more effective lubrication process.

Hydrocarbon oil such as mineral oil may be added to the granules as spray or in solvent solution.

Disintegrants

- Is a substance, or a mixture of substances, added to a tablet to facilitate its breakup or disintegration after administration. dintegrant may function by drawing water into the tablet ,swelling and causing the tablet to burst apart.
- Materials serving as **disintegrants** are starch (5-20% of tablet weight),Primogel and Explotab(substituted carboxymethylstarch)1-8% and 4% is reported as optimum. Clays like veegum and bentonite in about 10%(their use is limited unless tablet is colored since clays produce off-white appearance), pregelatinized starch 5% concentration and cross-linked polymer like crosscarmellose sodium(AC-Di-Sol cross linked from sodium carboxymethylcelullose) and crosslinked polyvinylpyrrolidone.

- The oldest and still the most popular disintegrants are **corn and potato starch** which have been well-dried and powdered.

- **Starch has a great affinity for water and swells when moistened, thus facilitating the rupture of the tablet matrix.**

- Others suggested that its disintegrating action in tablets is due to **capillary action rather than swelling.**

- **Starch 5%** is suggested, but if more rapid disintegration is desired, this amount may be increased to **10 or 15%.**

- Usually disintegration time would **decrease** as the percentage of **starch increased**.

- A group of materials such as Croscarmelose, crospovidone and sodium starch glycolate known as **super disintegrants**

WHY ??

- This name comes from the low levels (2 to 4%) at which they are completely effective . When they come in contact with water in oral cavity/GIT break down in to small particles.
- 1. Modified starches (Sodium starch glycolate, NF) Description: Sodium carboxy methyl starch; the carboxy methyl groups induces hydrophilicity and crosslinking reduces solubility. Trade name: Explotab®, Primojel® , Tablo®
- 2. Modified cellulose (Croscarmellose, NF) Description: Sodium carboxymethyl cellulose which has been cross-linked to render the material insoluble. Trade name: AcDiSol®,Primellose®
- 3. Cross-linked poly-vinyl pyrrolidone (Crospovidone, NF) Description: Cross-linked poly vinyl pyrrolidone; cross-linking render the material insoluble in water.
- Sodium starch glycolate swells 7-12 fold in less than 30 seconds.
- Croscarmelose swells 4-8 fold in less than 10 seconds.

- The disintegrating agent usually is mixed with the active ingredients and diluents **prior to granulation**.
- In some cases it may be advantageous to divide starch into two portions:

One part is added to the powdered formula **prior to granulation**,

and the **remainder** is mixed with the lubricant and added **prior to compression**.

Incorporated in this manner, like **starch serves a double purpose**; the portion added to the lubricant **rapidly breaks down the tablet to granules**, and the starch mixed with the active ingredients **disintegrates the granules into smaller particles**.

- **Other factors than the presence of disintegrants can affect significantly the disintegration time of compressed tablets:**

1- The binder

2- Tablet hardness

3- Lubricant.

4- Evolution of carbon dioxide. As in effervescent tablets.

Colors and dyes serve to:

1. Disguise off-color drugs.
2. Provide product identification.
3. Produce a more elegant product.

Food, drug, and cosmetic FD&C and D&C dyes are applied as **solutions in granulating agent; lakes which define as** dyes that have been absorbed on a hydrous oxide are usually employed as dry powders.

- When wet granulation is employed , care should be taken to prevent color migration during drying.Also the formulation should be checked for resistance to color change on exposure to light .Artificial light source are available to stimulate ultraviolet spectrum of sun light.

Flavoring agents

Are usually limited to chewable tablets or tablets intended to dissolve in the mouth.

- **(a)** Generally, water-soluble flavors have poor stability; hence, flavor oils or dry powders usually are used.

- **(b)** Flavor oils may be added to tablet granulations in solvents, dispersed on clays and other adsorbents, or emulsified in aqueous granulating agents.
- Usually, the maximum amount of oil that can be added to a granulation without influencing its tablet characteristics is **O.5%—O.75%.**

- **Artificial sweeteners**, like flavors, are usually used only with chewable tablets or tablets dissolve in the mouth.

(a) Some sweetness may come from the diluent (**e.g., mannitol, lactose**); agents, such as **saccharin and aspartame**, can also be added.

(b) **Saccharin** has an unpleasant after taste.

(c) **Aspartame** is not stable in the presence of moisture.

- **Adsorbents**

(e.g., magnesium oxide, magnesium carbonate, bentonit, silicon dioxide) are substances capable of holding quantities of fluid in an apparently dry state.

Characteristics of ideal tablets

1. **Free of defects ,such as chips ,cracks ,discoloration &contamination.**

2. **Have the strength to withstand the mechanical stress of production.**

3. **Chemically & physically stable over time.**

4. **Release the medicinal agents in a predictable& reproducible manner .**

ADVANTAGES OF GRANULATION PROCESS

WET GRANULATION	DRY GRANULATION	DIRECT COMPRESSION
❑ Improved flow by increasing particle size ❑ Uniform distribution of API, colour etc. – improved content uniformity ❑ Good for bulky powders, less dust and environmental contamination ❑ Lower compression pressure, less wear and tear on tooling	❑ Improved flow by increasing particle size ❑ Improved cohesion during compression ❑ Granulation without addition of liquid	❑ Fewer processing steps – blending and compression -reduced processing time ❑ Processing without moisture and heat – fewer stability problems ❑ Rapid and most direct method of tablet compression

Table 1 - Key Tablet Manufacturing Processes		
Manufacturing method	**Applicability**	**Comments**
Direct compression	Low and intermediate drug contents (usually 2-30%)	Not suitable for very low or high drug contents. Susceptible to variations in drug substance properties.
Dry granulation	Low to high drug content depending on drug substance properties	Avoids the use of water. Some limitations on utility dependent on the properties of the drug substance.
Wet granulation	All drug contents (from very low to very high)	Flexible but resource intensive process which is hard to automate. Usually uses water in the manufacturing process so may not be suitable for moisture sensitive products

TABLETS

Methods Tablet Preparations

General methods of tablet preparation:

❖ Wet Granulation

- The most widely used and most general method, why???
- This due to the greater probability that the granulation will meet all the physical requirements for the compression of good tablets.
- Its chief disadvantages are the number of separate steps involved, as well as the time and labor necessary to carry out the procedure, especially on a large scale.

The steps in the wet method are:

1-weighing, 2-mixing, 3-granulation, 4-screening the damp mass

5- drying, 6-dry screening, 7-lubrication and 8-compression.

- **THE GENERAL STEPS INVOLVED:**

1. The active ingredient, diluent and disintegrant are mixed or blended well.

2. The powder blend may be sifted through a screen, **WHY?**

To remove or break up lumps, this screening affords additional mixing.

NOTE:

The screen selected always should not affect the **potency of the ingredients,**

HOW??through interaction. **For example**, the stability of ascorbic acid is affected deleteriously by even small amounts of copper, thus care must be taken **to avoid contact with copper or copper-containing alloys**

3. Solutions of the binding agent are added to the mixed powders with stirring.

4. The powder mass is **wetted** with the binding solution until the mass has the consistency of **damp snow or brown sugar(Check by Ball test).**

NOTE:

- If the granulation is **over wetted**, the granules will be **hard**, requiring considerable pressure to form the tablets, and the resultant tablets may have **a mottled appearance**.
- If the powder mixture is **not wetted sufficiently**, the resulting granules will be **too soft**, breaking down during lubrication and **causing difficulty during compression.**

5. Screening of the wetted mass through certain seive according to the required granulation size needed **(mesh no.) .**

6. Drying of the resulted granules using suitable dryer .

- **In the past, Tray dryer(traditional static bed dryer)** was the most widely used method for drying of tablet granulations.
- **In fluidized bed dryer(newer and efficient dryer**), the granules are suspended and agitated in a warm air stream(granules are boiled through heated air stream).

The fluidization method have advantages such as :

1. Decreased drying time(by Comparing the fluidized bed and a tray dryer indicated that the former was **15 times** faster than the conventional method of tray drying).

2. Better control of drying temperatures.

3. Decreased handling costs .

4. The opportunity to blend lubricants and other materials with the dry granules directly in the fluidized bed.

- **NOTE:**

In drying,it is desirable to maintain **a residual amount of moisture** in the granulation,**WHY? ??**

1. This is necessary to maintain the various granulation ingredients such as gums in a **hydrated state.**

2. The residual moisture contributes to the reduction of the **static electric charges** on the particles.

So in the selection of any drying process, an effort is made to obtain a uniform moisture content,(How to calculate MC%)?

Q// THE MOISTURE CONTAINT SHOULD BE CALCULATED DURING PREPARATION OF TABLET?

In addition to the importance of moisture content of the granulation in its **handling during the manufacturing steps**, the stability of the products containing **moisture-sensitive active ingredients** may be related to the moisture content of the products.

NOTE:

Previously it was indicated that **water-soluble colorants** can migrate toward the surface of the granules during the drying process, resulting in **mottled tablets** after compression.

This is also true for **water-soluble drug substances**, resulting in tablets unsatisfactory as **to content uniformity**.

Q//HOW TO SOLVE THIS PROBLEM ??

Migration can be reduced by drying the granulation slowly at low temperatures or **by using a granulation in which the major diluent is present as granules of large particle size**.

The presence of **microcrystalline cellulose** in wet granulations also reduces migration tendencies.

7. After drying, the granulation is reduced in size by passing through screen.

8. After dry granulation, the lubricant is added as a fine powder (It is usually screened through 60- or 100-mesh nylon cloth) **WHY??**

To eliminate **small lumps** as well as to **increase the covering power** of the lubricant.

NOTE:

The presence of some fines is necessary **for the proper filling of the die cavity.**

- # Dry Granulation

- **When tablet ingredients are sensitive to moisture or are unable to withstand elevated temperatures during drying, and when the tablet ingredients have sufficient inherent binding or cohesive properties, slugging may be used to form granules.**

- **This method is referred to as dry granulation, pre compression or double-compression. It eliminates a number of steps but still includes weighing, mixing, slugging, dry screening, lubrication and compression.**

- **The compressed slugs are comminuted through the desirable mesh screen either by hand, or for larger quantities through the comminuting mill.**
- **The lubricant remaining is added to the granulation, blended gently and the material is compressed into tablets.**
- **Aspirin is a good example where slugging is satisfactory.**

Direct Compression

- **Direct compression consists of compressing tablets directly from powdered material without modifying the physical nature of the material itself.**

1. **Reserved for a small group of crystalline chemicals having all the physical characteristics required for the formation of a good tablet. This group includes chemicals such as potassium salts (chlorate, chloride, bromide, iodide, nitrate, permanganate), ammonium chloride.**

2. **For tablets in which the drug itself constitutes a major portion of the total tablet weight,** it is necessary that the drug possess those physical characteristics required for the formulation to be compressed directly.

3.Direct compression for tablets containing 25% or less of drug substances frequently can be used by formulating with a suitable **diluent** which acts as a **carrier or vehicle** for the drug.

- These properties are imparted to them by **a preprocessing step ,HOW???**

  By wet granulation, slugging, spray drying, or crystallization.

- These vehicles include **processed forms of most of the common diluents** including dicalcium phosphate dihydrate, tricalcium phosphate, calcium sulfate, anhydrous lactose, spray-dried lactose, pregelatinized starch, compressible sugar, mannitol and microcrystalline cellulose.

- **These commercially available direct- compression vehicles** may contain small quantities of other ingredients , **WHY?? (e.g, starch)** as processing aids.

- **Dicalcium phosphate dihydrate (Di-Tab,)**

The chemical is odorless, tasteless and non- hygroscopic. Since it has no inherent lubricating or disintegrating properties, that was other additives must be present to prepare a satisfactory formulation ,**WHY???**

- ***Compressible sugar***

It is a white crystalline powder with a sweet taste and complete water solubility ,*consists mainly of sucrose that is processed to have properties suitable* for direct compression. It also may contain small quantities of dextrin, starch or invert sugar.

- It requires the incorporation of a **suitable lubricant** at normal levels for lubricity. The sugar is used widely for chewable vitamin tablets, **WHY??** because of its natural sweetness.

One commercial source is Di-Pac (Amstar):

Which is prepared by the cocrystallization of 97% sucrose and 3% dextrins.

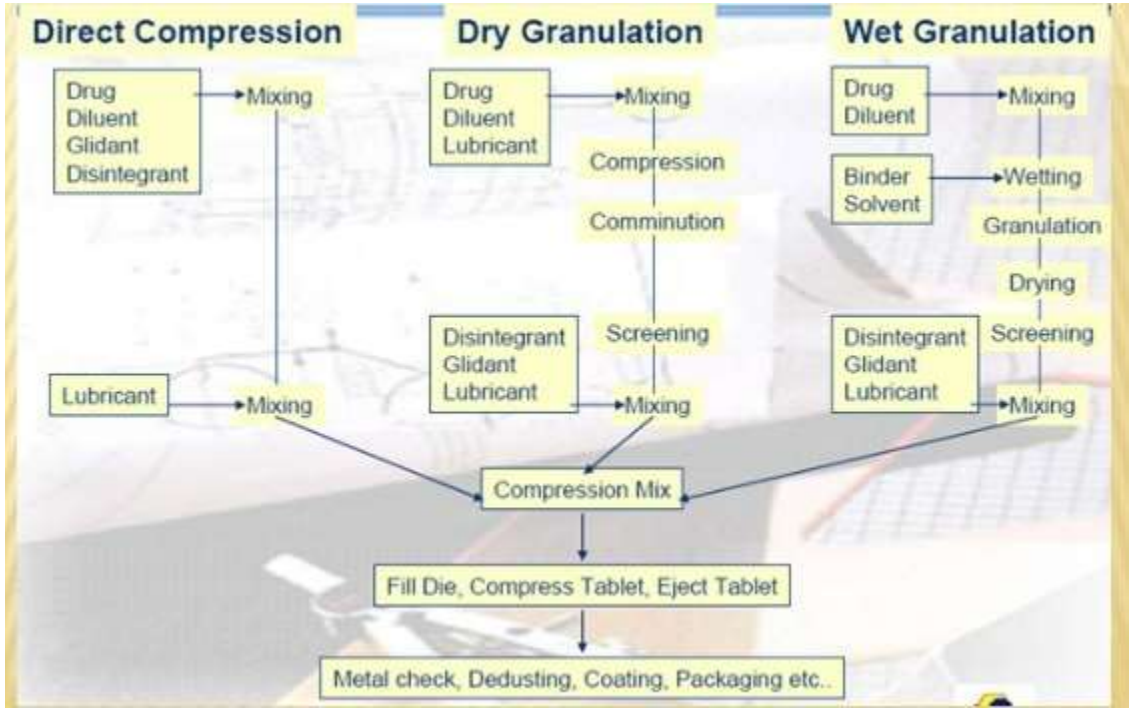
- Some forms of lactose meet the requirements for a direct-compression vehicle, **Both anhydrous lactose and spray dried lactose have good flowability and compressibility** and can be used in direct compression.

Hydrous lactose does not flow so that ,its use is limited to tablet formulations prepared by the wet granulation method

- **microcrystalline cellulose (Avicel, FMC).**

This non fibrous form of cellulose is obtained by spray-drying washed, acid-treated cellulose and is available in several grades which range in average particle size from 20 to 100 um. It is water insoluble but the material has the ability to draw fluid into a tablet by capillary action;

It swells on contact and thus acts as a disintegrating agent. The material flows well and has a degree of self-lubricating qualities, thus requiring a lower level of lubricant as compared to other excipients **,WHY???.**


Direct Compression
Dry Granulation
Wet Granulation
Drug
Diluent
Glidant
Disintegrant
Mixing
Lubricant
Mixing
Drug
Diluent
Lubricant
Mixing
Compression
Comminution
Disintegrant
Glidant
Lubricant
Screening
Mixing
Drug
Diluent
Mixing
Binder
Solvent
Wetting
Granulation
Drying
Disintegrant
Glidant
Lubricant
Screening
Mixing
Compression Mix
Fill Die, Compress Tablet, Eject Tablet
Metal check, Dedusting, Coating, Packaging etc..