TABLETS

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Topics to be covered...

- **Conventional Tablets:**
  - Formulation of different types of tablets,
  - Granulation technology on large-scale by various techniques,
  - Physics of tablets making,
  - Different types of tablet compression machinery & equipments employed,
  - Evaluation of tablets.

- **Coating of tablets:**
  - Types of Coating,
  - Film Forming Materials,
  - Formulation of Coating Solution,
  - Equipments for Coating,
  - Coating process, evaluation of coated tablets.
History of tablet dosage form

- 1843: a patent was granted to Thomas Brockedon (Englishman) for manufacturing pills and lozenges
- 1874: both rotary and eccentric presses
- 1885: Glyceryl trinitrate tablets was in the BP
- No other tablet monograph appeared until 1945
- 1980: nearly 300 monographs for tablets
Introduction of Tablets

- The **oral route is the most common way** of administering drugs.
- **Amongst** the oral dosage form tablets are the most common. (~90% Market share)
- Formulating a **solid dosage form by powder compression** is not new.
- A tablet **consists of one or more drugs** (active ingredients) as well as a **series of other substances** used in the formulation of a **complete preparation.**
Introduction of Tablets

- Defn: Tablets are defined as *unit dose, temper evident solid preparations containing one or more active ingredients*.
- Tablets are obtained by compressing uniform volumes of particles.
- Most of time powders must be converted to *granules*.
Introduction of Tablets

- They are *mainly intended for oral administration*.
- Some are
  - Swallowed whole (Conventional)
  - Some are being *chewed* (Chewable)
  - Some are *dissolved or dispersed in water* before being administered (Dispersible)
  - Some are *retained in the mouth*, where the active ingredient is 'liberated'. (Buccal & Sublingual)
Why tablets are more popular??

- Oral route - convenient and safe way of drug administration.
- Advantage of the chemical and physical stability
- It enables accurate dosing of the drug.
- Convenient to handle
- Mass production is not cumbersome.
- Robust and quality-controlled production gives consistent quality
- Low price.
Advantages of Tablets

- Tablets are convenient to use and are an elegant dosage form.
- Offers a range of drug release rates and durations of clinical effect.
- Tablets may be formulated to offer rapid drug release or controlled drug release.
- Gives formulator choice to release the therapeutic agent at a particular site within the gastrointestinal tract
  - To reduce side effects
  - To promote absorption at that site and
  - To provide a local effect
Advantages of Tablets

- Physical or chemical incompatible active pharmaceutical substances can be incorporated.
- The release of each therapeutic agent may be effectively controlled by formulation and design.
- Except proteinaceous drugs, all classes of therapeutic agents may be administered.
- Easier to mask the taste of bitter drugs.
- The Superior chemical, physical and microbiological stability
- Inexpensive dosage form.
Advantages of Tablets

- **Production aspect**
  - Large scale production at lowest cost
  - Easiest and cheapest to package and ship
  - High stability

- **User aspect (doctor, pharmacist, patient)**
  - Easy to handling
  - Lightest and most compact
  - Greatest dose precision & least content variability
  - Coating can mark unpleasant tastes & improve pt. acceptability
Disadvantages of Tablets

- It requires a series of unit operations, causing increased level of product loss.
- The absorption dependent on physiological factors, e.g. gastric emptying rate, and shows inter patient variation.
- The compression properties of certain therapeutic agents are poor.
- Impose problem for administering in children and the elderly - difficulties in swallowing.
Disadvantages of Tablets

- Some drugs resist compression into dense compacts
- Drugs with poor wetting, slow dissolution, intermediate to large dosages may be difficult or impossible to formulate and manufacture as a tablet that provide adequate or full drug bioavailability
- Bitter taste drugs, drugs with an objectionable odor, or sensitive to oxygen or moisture may require encapsulation or entrapment prior to compression or the tablets may require coating
Types of Tablets

- Tablet may be
  - uncoated or coated.

- **Coated tablets:**
  - enteric coated tablet,
  - film coated tablet,
  - implant,
  - sugar coated tablet and modified-release tablet.

- **Uncoated tablets:**
  - chewable tablet,
  - effervescent tablet,
  - lozenge tablet,
  - soluble tablet and sublingual tablet.
Types of tablets

- **Route of administration**
  - Oral tablets
  - Sublingual or buccal tablets
  - Vaginal tablets

- **Production process**
  - Compressed tablets
  - Multiple compressed tablets
    - Tablet within a tablets: core and shell
    - Multilayer tablet
Types of tablets

- **Sugar coated tablets**
  - Protect tablets from moisture
  - Mask odor and flavor
  - Elegance

- **Film coated tablets**
  - Thin film coat
  - Soluble or insoluble polymer film

- **Chewable tablets**
  - Rapid disintegrate
  - Antacid, flatulence: rapid action
  - Children drug

- **Effervescient tablets**
  - Dissolve in the water before drink
Coating: Why???

- A broken section of a coated tablet shows a core which is surrounded by a continuous layer of a different texture. The reasons for coating a tablet are:
  - to protect the active ingredients from air, moisture, light,
  - to mask the unpleasant tastes and odor; and
  - to improve appearance
Coating: Why?
Essential properties of tablets

- **Accurate dosage** of medicament, uniform in weight, appearance and diameter
- Have the **strength** to withstand the rigors of mechanical shocks encountered in its production, packaging, shipping and dispensing
- **Release** the medicinal agents in the body in a predictable and reproducible manner
- Elegant product, acceptable size and shape
- Chemical and physical **stabilities**.
Types based on use

- **Ingested orally**
  - Compressed tablet
  - Multiple compressed tablet
  - Modified release tablets
  - Enteric coated tablets
  - Sugar coated tablet
  - Film coated tablet
  - Chewable tablet
  - Targeted tablets

- **Administered by other route**
  - Implants
  - Vaginal tablet

- **Used in oral cavity**
  - Buccal tablet
  - Sublingual tablet
  - Lozenges
  - Dental cone

- **Used to prepare solution**
  - Effervescent tablet
  - Dispensing tablet
  - Hypodermic tablet
Multiple compressed tablets

- **Reasons:**
  - to separate physically or chemically incompatible ingredients &
  - to produce repeat action/ prolonged action tablet.

- The tablet manufacturing machine is generally operated at relatively lower speed than for standard compression tablet.

- There are three categories under this class:
  - Layered tablets – two to three component system.
  - Compression coated tablets – tablet within a tablet.
  - Inlay tablet – coat partially surrounding the core.

- The layered tablet is preferred over compression coated tablet as the surface contact is less and the production is simple and more rapid.
Multilayered tablets

- **Reason:**
  - When two or more active pharmaceutical ingredients are needed to be administered simultaneously and they are incompatible, the best option for the formulation pharmacist would be to formulate multilayered tablet.

- It consists of several different granulations that are compressed to form a single tablet composed of two or more layers and usually each layer is of different color to produce a distinctive looking tablet.

- Each layer is fed from separate feed frame with individual weight control. Dust extraction is essential during compression to avoid contamination. Therefore, each layer undergoes light compression as each component is laid down. This avoids granules intermixing if the machine vibrates.

- For example,
  - Admixture containing Phenylephedrin HCL and Ascorbic Acid with Paracetamol.
  - Paracetamol + phenylephedrine Hydrochloride → one layer
  - Paracetamol + ascorbic acid → another layer.
Compression coated tablets

- Two parts, internal core and surrounding coat. Core is small porous tablet and prepared on one turret. For preparing final tablet, a bigger die cavity in another turret is used in which first the coat material is filled to half and then core tablet is mechanically transferred, again the remaining space is filled with coat material and finally compression force is applied.

- This tablet readily lend itself in to a repeat action tablet as the outer layer provides the initial dose while the inner core release the drug later on. But, when the core quickly releases the drug, entirely different blood level is achieved with the risk of over dose toxicity.

- To avoid immediate release of both the layers, the core tablet is coated with enteric polymer so that it will not release the drug in stomach while, the first dose is added in outer sugar coating.
Inlay tablets

- A type of layered tablet in which instead the core tablet being completely surrounded by coating, top surface is completely exposed. While preparation, only the bottom of the die cavity is filled with coating material and core is placed upon it.
- When compression force is applied, some coating material is displaced to form the sides and compress the whole tablet.
- It has some advantages over compression coated tablets:
  - Less coating material is required.
  - Core is visible, so coreless tablets can be easily detected.
  - Reduction in coating forms a thinner tablet and thus freedom from capping of top coating.
Chewable tablet

- The tablet which is intended to be broken and chewed in between the teeth before ingestion.
- Antacid and vitamin tablets are usually prepared as chewable tablets. It is given to the children who have difficulty in swallowing and to the adults who dislike swallowing.
Targeted tablets

- When we need to release the API at a specific site in the elementary tract, targeted drug delivery is a preferred option.
- Depending upon the composition and release mechanism of a tablet, the drug is delivered to a particular region.
- Two types of tablet:
  - Gastro retentive Tablet
  - Colonic tablets
Gastro retentive Tablet

- This type of dosage form is to be opted when API release is desired in stomach (Antacids, APIs used against H. pylori infection) or site of absorption is either stomach or upper part of small intestine.

- To retain the drug for longer time period in stomach, following approaches can be used:
  - Low density tablet (effervescent or non effervescent)
  - Tablets that can expand in gastric environment (swelling or by unfolding) and thus increasing the size so that it cannot cross the pyloric sphincter.
  - Using mucoadhesive polymers that stick to mucosa of stomach and provide slow drug release.

- Drugs like Diazepam, Levodopa and Ciprofloxacin are successfully marketed in this formulation.
Colonic tablets

- When the aim is to deliver the drug into colon without dilution in other regions of gastrointestinal tract or the drug has poor absorption in stomach or small intestine, colonic drug delivery is preferred.
- The pH in this region varies from 6.4 - 7 and presence of microbial flora plays as important role in drug release especially in this region.
- Various mechanisms are adopted for drug release in this area are coating with pH sensitive polymer e.g., Eudragit®S100, Eudragit® L100, biodegradable polymer like polymers which are sensitive to colonic bacteria, bioadhesive polymers which selectivity sticks to colonic mucosa e.g., polycarbophil or polyethans, redox sensitive polymers that respond to redox potential in colon which expresses total metabolic & bacterial action.
**Effervescent tablet**

- The tablet that contains acid substances and carbonate or hydrogen carbonate that react rapidly in the presence of water to release carbon dioxide.

- Sodium bicarbonate, citric acid and tartaric acid are added to the active ingredients to make the tablet effervescent. This preparation makes the tablet palatable.
Lozenge tablet

- The tablet that is intended to produce continuous effect on the mucous membrane of the throat.
- There is no disintegrating agent.
- The quality of the binding agent is increased so as to produce slow dissolution.
- Suitable sweetening (sugar), coloring and flavoring agents must be include in this formulation. Gum is used to give strength and cohesiveness to the lozenge and facilitating slow release of the active ingredient.
Soluble tablet

- The tablet that dissolves completely in liquid to produce solution of definite concentration.
- Mouth wash, gargle, skin lotion, douche; antibiotic, certain vitamins, and aspirin are given along with this formulation.
Sublingual tablet

- The drug which is destroyed or inactivated within the gastrointestinal tract but can be absorbed through the mucosal tissue of the oral cavity is usually given in this formulation.
- The tablet is required to be placed below the tongue for the slow release of drug.
- But for immediate effect some medicaments are formulated in such a way to dissolve within 1 to 2 minutes.
- Nitroglycerin is prepared in this formulation.
Enteric coated tablet

- Some drugs are destroyed by gastric juice or causes irritation to stomach. These two factors can be overcome by coating the tablet with cellulose acetate phthalate.
- This polymer is insoluble in gastric contents but readily dissolves in intestinal contents.
- So there is delay in the disintegration of dosage form until it reaches the small intestine.
- Like coated tablet, enteric coated tablet should be administered in whole form. Broken or crushed form of the enteric coated tablet causes destruction of the drug by gastric juice or irritation to the stomach.
- Enteric coated tablet is comparatively expensive.
Implant

- A small tablet that is prepared for insertion under the skin by giving a small surgical cut into the skin which is stitched after the insertion of the tablet.
- This tablet must be sterile.
- The drug used in this preparation is usually water insoluble and the tablet provides a slow and continuous release of drug over prolonged period of time ranging from 3 to 6 months or even more.
- Contraceptive tablet is formulated as implant.
Sugar coated tablet

- The tablet that contains active ingredient(s) of unpleasant taste may be covered with sugar to make it more palatable.
- This type of tablet should be administered in whole form, otherwise the patient will experience the unpleasant taste of the active ingredient.
Film coated tablet

- The tablet that is covered with a thin layer or film of polymeric substance which protects the drug from atmospheric conditions and mask the objectionable taste and the odor of drug.
Modified release tablet

- Modified-released tablet is either uncoated or coated.
- This contains special additives or prepared by special procedure which, separately or together, is intended to modify the rate of release of the drug into the gastrointestinal tract.
- It prolongs the effect of drug and also reduces the frequency of administration of drug.
- Several drugs are available in modified release tablet like indomethacin.
- There is another term popularly known as pill.
- Once the people’s idea was to use of pill in every ill. Now days the term has been only used in contraceptive preparations such as combination pill, minipill, and morning after pill.
Additives used in tablets

- Drugs
- Diluents
- Binders
- Disintegrants
- Lubricants
- Glidants
- Antiadherants
- Preservatives
- Coloring agents
- Flavoring agents
- Sweetening agent
Additives used in tablets: **Drugs**

- Active pharmaceutical ingredient (API), therapeutic agent
- Should not produce any toxic effect when come in contact with other additives,
- Accurate quantity as label claim,
- Detected by various methods of analysis
- Example: paracetamol, aspirin, diclofenac, metformin, telmisartan, nimesulide, nifedipine etc.
Additives used in tablets: **Diluent**

- Act as fillers used to make required bulk of the tablet
- Must provide better tablet properties such as improve cohesion, to permit use of direct compression manufacturing or to promote flow.
- A diluent should have following properties:
  - Non toxic
  - Commercially available in acceptable grade
  - Low in cost
  - Physiologically inert
  - Physically & chemically stable by themselves & in combination with the drugs.
  - Free from all microbial contamination.
  - Do not alter bioavailability of drug.
  - Color compatible
Additives used in tablets: **Diluent**

- **Commonly used tablet diluents**
  - Lactose-anhydrous and spray dried lactose
  - Directly compressed starch-Sta Rx 1500
  - Hydrolyzed starch-Emdex and Celutab
  - Microcrystalline cellulose-Avicel (PH 101 and PH 102)
  - Dibasic calcium phosphate dehydrate
  - Calcium sulphate dihydrate
  - Mannitol
  - Sorbitol
  - Sucrose- Sugartab, DiPac, Nutab
  - Dextrose
Additives used in tablets: **Binders**

- Binders hold the ingredients in a tablet together
- Binders ensure that tablets and granules can be formed with required mechanical strength
- Added either **dry or in wet-form** to form granules or cohesive compacts

**Examples:**

- Acacia, tragacanth- Solution for 10-25% Conc.
- Cellulose derivatives- MC, HPC, HPMC
- Gelatin- 10-20% solution , Glucose- 50% solution
- Polyvinylpyrrolidone (PVP)- 2% conc. , Starch paste-10-20% solution
- Sodium alginate , sorbitol , sugar alcohols like xylitol, sorbitol or maltitol.
Additives used in tablets: **Disintegrants**

- Added to facilitate disintegration when comes in contact with water in the GIT.
- Disintegrants expand and dissolve when wet causing the tablet to break apart in the digestive tract, releasing the active ingredients for absorption.

**Disintegrants type include:**
- Water uptake facilitators
- Tablet rupture promoters

They ensure that when the tablet is in contact with water, it rapidly breaks down into smaller fragments, thereby facilitating dissolution.

**Example:**
- Starch- 5-20% of tablet weight, Starch derivative – Primogel and Explotab (1-8%)
- Clays- Veegum HV, bentonite 10% level in colored tablet, Alginates,
- Cellulose derivatives- Ac-Di-Sol (sodium carboxy methyl cellulose), PVP (cross-linked)
Additives used in tablets: **Lubricants**

- Lubricants prevent ingredients from clumping together and from sticking to the tablet punches or capsule filling machine.
- Lubricants also ensure that tablet formation and injection can occur with low friction between the solid and die wall.
- Used to prevent adhesion of the tablet materials to the surface of dies and punches,
- Reduce inter particle friction and may improve the rate of flow of the tablet granulation.
- **Example:** Stearic acid, Magnesium stearate, Talc, PEG, Surfactants
Additives used in tablets: **Glidants**

- Glidants are intended to **promote flow of granules or powder material by reducing the friction between the particles**.
- Glidants are used to improve the flowability of the powder or granules or both.
- **Example: Corn Starch – 5-10% conc., Talc-5% conc., Silica derivative** - Colloidal silicas such as Cab-O-Sil, Syloid, Aerosil in 0.25-3% conc.
Additives used in tablets: **Antiadherants**

- Reduce the adhesion between the powder (granules) and the punch faces and thus prevent tablet sticking to the tablet punches.
**Additives used in tablets: Preservatives**

- Some typical preservatives used in pharmaceutical formulations are.

- **Examples:**
  - Vitamin A, vitamin E, vitamin C, retinyl palmitate,
  - amino acids like cysteine, methionine,
  - citric acid and sodium citrate
  - synthetic preservatives like methyl paraben and propyl paraben.
Additives used in tablets: Coloring agents

- All coloring agents must be approved and certified by FDA.
- Two forms of colors are used in tablet preparation – FD &C and D & C dyes.
- Lakes are dyes absorbed on hydrous oxide and employed as dry powder coloring.
  - Example: FD & C yellow 6-sunset yellow
  - FD & C yellow 5- Tartrazine
  - FD & C green 3- Fast Green
  - FD & C blue 1- Brilliant Blue
  - FD & C blue 2 - Indigo carmine
  - D & C red 3- Erythrosine.
  - D & C red 22 – Eosin Y
Additives used in tablets: **Flavoring agents**

- **Flavoring agents**: For chewable tablet- flavor oil are used
- Flavors are added to improve the taste or appearance of a formulation.
Additives used in tablets: **Sweeteners**

- Sweeteners are added to make the ingredients more palatable, especially in chewable tablets such as antacid or liquids like cough syrup.
- Therefore, tooth decay is sometimes associated with cough syrup abuse.
- Sugar can be used to disguise unpleasant tastes or smells.
- **Sweetening agents**: For chewable tablets: Sugar, mannitol.
- Saccharine (artificial): 500 time’s sweeter than sucrose
- Disadvantage: Bitter aftertaste and carcinogenic
- Aspartame (artificial)
- Disadvantage: Lack of stability in presence of moisture.
Granulation

- A size enlargement process which converts small particles into physically stronger & larger agglomerates.
- Granulation method can be broadly classified into three types:
  - Wet granulation
  - Dry granulation
  - Direct compression
Granulation

- Ideal characteristics of granules
  - spherical shape,
  - smaller particle size distribution with sufficient fines to fill void spaces between granules,
  - adequate moisture (between 1-2%),
  - good flow,
  - good compressibility and
  - sufficient hardness.
Granulation

- The effectiveness of granulation depends on the following properties
  i) Particle size of the drug and excipients
  ii) Type of binder (strong or weak)
  iii) Volume of binder (less or more)
  iv) Wet massing time (less or more)
  v) Amount of shear applied
  vi) Drying rate (Hydrate formation and polymorphism)
Wet granulation

- The most widely used process of agglomeration (granulation) in pharmaceutical industry is wet granulation.

- Wet granulation process simply involves wet massing of the powder blend with a granulating liquid, wet sizing and drying.
Important steps involved in the wet granulation

1. Mixing of the drug(s) and excipients
2. Preparation of binder solution
3. Mixing of binder solution with powder mixture to form wet mass.
   - Coarse screening of wet mass using a suitable sieve (6-12)
4. Drying of moist granules.
   - Screening of dry granules through a suitable sieve (14-20)
5. Mixing of screened granules with disintegrant, glidant, and lubricant.
Limitation of Wet Granulation

i) Cost: It is an expensive process because of labor, time, equipment, energy and space requirements.

ii) Loss of material during various stages of processing

iii) Stability may be major concern for moisture sensitive or thermo labile drugs

iv) Multiple processing steps add complexity and make validation and control difficult

v) An inherent limitation of wet granulation is that any incompatibility between formulation components is aggravated.
Dry Granulation

- In dry granulation process the powder mixture is compressed without the use of heat and solvent.

- It is the least desirable of all methods of granulation. The two basic procedures are to form a compact of material by compression and then to mill the compact to obtain a granules.

- Two methods are used for dry granulation.
  - The more widely used method is slugging, where the powder is precompressed and the resulting tablet or slug are milled to yield the granules.
  - The other method is to precompress the powder with pressure rolls using a machine such as Chilosonator.
Advantages of dry granulation

- Less equipments and space.
- It eliminates the need for binder solution, heavy mixing equipment and the costly and time consuming drying step required for wet granulation.
- Slugging can be used for advantages in the following situations:
  - For moisture sensitive material
  - For heat sensitive material
  - For improved disintegration since powder particles are not bonded together by a binder
Disadvantages of dry granulation

i) It requires a specialized heavy duty tablet press to form slug

ii) It does not permit uniform colour distribution as can be achieved with wet granulation where the dye can be incorporated into binder liquid.

iii) The process tends to create more dust than wet granulation, increasing the potential contamination
Important steps involved in the dry granulation

Milling of drugs and excipients

Mixing of milled powders

Compression into large, hard tablets to make slug

# Screening of slugs

Mixing with lubricant and disintegrating agent

Tablet compression
GENERAL PROCESS OF TABLET MANUFACTURING

1. Active ingredient
2. Excipients (ingredients to bind the active elements together)
3. Mixing and granulation
4. Drying
5. Pressing
6. Coating
7. Packaging
Direct Compression

- In this method only blending & compression is involved.
- **Advantages:**
  - Increased output,
  - Reduced costs,
  - Less machinery,
  - Improved drug stability,
  - Faster dissolution of drugs,
  - Less wear & tear of punches,
  - Simplified validation.
- **Disadvantages:**
  - Segregation: problems arise in weight variation & content uniformity.
  - Cost: as the directly compressible excipients are costly the cost of tablet is more.
  - Low dilution potential: as the active material is only 30-40\% as the requirement of excipient, it is difficult for the patients to swallow.
  - Not useful for drugs having poor flow properties or low bulk density.
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<tr>
<th>Step</th>
<th>Wet granulation</th>
<th>Dry granulation</th>
<th>Direct compression</th>
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<td>1</td>
<td>Mixing &amp; blending of API &amp; excipients</td>
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<td>2</td>
<td>Preparation of binder solution</td>
<td>Compression in to slug</td>
<td>Compression</td>
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<td>3</td>
<td>Massing of binder solution of step 2</td>
<td>Size reduction of slug &amp; sieving</td>
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<td>with powder mixture of step 1</td>
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<td>4</td>
<td>Wet screening of damp mass</td>
<td>Mixing of granules with p’ceutical aids</td>
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<td>Drying of wet granules</td>
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<td>Resifting of dried granules &amp; blending</td>
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<td>with p’ceutical aids</td>
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<td>7</td>
<td>Compression</td>
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</table>
Reasons for Granulation

- To **prevent segregation** of the constituents of the powder mix.
  - Segregation (or demixing) is due primarily to **differences in**
    the size or density of the components of the mix.
  - The **smaller and/or denser particles** concentrating at the
    base of a container
  - The **larger and/or less dense ones above them**.
  - An **ideal granulation will contain all the constituents of the**
    **mix in the correct proportion** in each granule and
    segregation of the ingredients will not occur.
Reasons for Granulation

- To **improve the flow properties** of the mix
  - Many powders, because of their small size, irregular shape or surface characteristics, are cohesive and do not flow well.
  - Poor flow will often result in a **wide weight variation** within the final product owing to variable fill of tablet dies etc.
Reasons for Granulation

- To improve the compaction characteristics of the mix
  - Some powders are difficult to compact even if a readily compactable adhesive is included in the mix and some are compacted easily.
  - Solute migration occurring during the post granulation drying stage results in a binder-rich outer layer to the granules.
  - This in turn leads to direct binder–binder bonding, which assists the consolidation of weakly bonding materials.
Reasons for Granulation

- Other Reasons:
  - The granulation of toxic materials will reduce the hazard associated with the generation of toxic dust that may arise when handling powders.
  - Materials which are slightly hygroscopic may adhere and form a cake if stored as a powder. Granulation may reduce this hazard, as the granules will be able to absorb some moisture and retain their flow ability because of their size.
  - Granules, being denser than the parent powder mix, occupy less volume per unit weight. They are therefore more convenient for storage or shipment.
Granulation Mechanisms

- To form granules, bonds must be formed between powder particles so that they adhere and these bonds must be sufficiently strong to prevent breakdown of the granule to powder in subsequent handling operations.

- Five primary bonding mechanisms between particles:
  - Adhesion and cohesion forces in the immobile liquid films
  - Interfacial forces in mobile liquid films.
  - Formation of solid bridges after solvent evaporation
  - Attractive forces between solid particles
  - Mechanical interlocking
Granulation Mechanisms

- **At low moisture levels**, termed the **pendular state**, the particles are held together by lens-shaped rings of liquid.
- **When all the air has been displaced** from between the particles the **capillary state** is reached, and the particles are held by capillary suction at the liquid/air interface.
Granulation Mechanisms

- The funicular state represents an intermediate stage between the pendular and capillary states.
- Moist granule tensile strength increases about three times between the pendular and the capillary state.
Pharmaceutical Granulation Equipment

- **Wet granulators:**
  - There are three main types of granulator used in the pharmaceutical industry for wet granulation.
    - Shear granulators
    - High-speed mixer/granulators
    - Fluidized-bed granulators
Shear Granulators

- The mixed powders are fed into the bowl of the planetary mixer and granulating liquid is added as the paddle of the mixer agitates the powders.
- The planetary action of the blade when mixing is similar to that of a household mixer.
Shear Granulators

- The rotor bars of the granulator oscillate and force the moist mass through the sieve screen, the size of which determines the granule size.
- The mass should be sufficiently moist to form discrete granules.
- If excess liquid is added, strings of material will be formed.
- If the mix is too dry the mass will be sieved to powder and granules will not be formed.
Shear Granulators

- The **disadvantages** are as follow:
  - Long duration
  - Need for **several pieces of equipment**, 
  - **High material losses** that can be incurred because of the transfer stages.
High-speed mixer/granulators

- This type of granulator (e.g. Diosna, Fielder) is used extensively in pharmaceutics.

- The machines have a
  - Stainless steel mixing bowl containing a three-bladed main impeller, which revolves in the horizontal plane,
  - Three-bladed auxiliary chopper (breaker blade) which revolves either in the vertical or the horizontal plane
High-speed mixers

- The unmixed dry powders are placed in the bowl and mixed by the rotating impeller for a few minutes.
- Granulating liquid is then added via a port in the lid of the granulator while the impeller is turning.
- The granulating fluid is mixed into the powders by the impeller.
High-speed mixers

- The chopper is usually switched on when the moist mass is formed, as its function is to break up the wet mass to produce a bed of granular material.
- Once a satisfactory granule has been produced, the granular product is discharged, passing through a wire mesh which breaks up any large aggregates.
- The advantage of the process is that
  - mixing,
  - massing and
  - granulation
- all are performed within a few minutes in same piece of equipment.
High-speed mixers

- Collette-gral mixer is a modification of Diosna Mixer.
- This is based on the bowl and overhead drive of the planetary mixer.
- It consist of three blades, which rotate in the horizontal plane at the base of the bowl,
- and the second carries smaller blades which act as the chopper and rotate in the horizontal plane in the upper regions of the granulating mass.
Fluidized-bed granulators

- The powder particles are fluidized in a stream of air, but in addition granulation fluid is sprayed from a nozzle on to the bed of powders.
- Heated and filtered air is blown or sucked through the bed of unmixed powders to fluidize the particles and mix the powders; fluidization is actually a very efficient mixing process.
Fluidized-bed granulators

- Granulating fluid is pumped from a reservoir through a spray nozzle positioned over the bed of particles.
- The fluid causes the primary powder particles to adhere when the droplets and powders collide.
- Escape of material from the granulation chamber is prevented by exhaust filters, which are periodically agitated to reintroduce the collected material into the fluidized bed.
Fluidized-bed granulators

- **Advantages:**
  - All the granulation processes are performed in one unit,
  - Saving labour costs,
  - Saving transfer losses and time.
  - Process can be automated once the conditions affecting the granulation have been optimized

- **Disadvantages:**
  - Initially expensive and
  - Optimization of process (and product) parameters affecting granulation needs extensive development work
<table>
<thead>
<tr>
<th>Apparatus parameters</th>
<th>Process parameters</th>
<th>Product parameters</th>
</tr>
</thead>
<tbody>
<tr>
<td>Air distribution plate</td>
<td>Bed load</td>
<td>Type of binder</td>
</tr>
<tr>
<td>Shape of granulator body</td>
<td>Fluidizing air flow rate</td>
<td>Quantity of binder</td>
</tr>
<tr>
<td>Nozzle height</td>
<td>Fluidizing air temperature</td>
<td>Binder solvent</td>
</tr>
<tr>
<td>Positive or negative pressure operation</td>
<td>Fluidizing air humidity</td>
<td>Concentration of granulating solution</td>
</tr>
<tr>
<td>Scale-up</td>
<td>Atomization</td>
<td>Temperature of granulation solution</td>
</tr>
<tr>
<td></td>
<td>Nozzle type</td>
<td>Starting Materials</td>
</tr>
<tr>
<td></td>
<td>Spray angle</td>
<td>Fluidization</td>
</tr>
<tr>
<td></td>
<td>Spraying regime</td>
<td>Powder hydrophobicity</td>
</tr>
<tr>
<td></td>
<td>Liquid flow rate</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Atomizing air flow rate</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Atomizing air pressure</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Droplet size</td>
<td></td>
</tr>
</tbody>
</table>
Dry granulators

- Dry granulation converts primary powder particles into granules using the application of pressure without the intermediate use of a liquid.
- It therefore avoids heat-temperature combinations that might cause degradation of the product.
- The method is also know as slugging
- Two pieces of equipment are necessary for dry granulation:
  - First, a machine for compressing the dry powders into compacts or flakes, and
  - Secondly a mill for breaking up these intermediate products into granules.
Dry granulators

- **Sluggers:**
  - Dry powders can be compressed using a conventional tablet machine or, more usually, a large heavy duty rotary press can be used.
  - This process is often known as 'slugging'.
  - A hammer mill is suitable for breaking the compacts.

- **Roller compactors:**
  - Powder mix being squeezed between two rollers to form a compressed sheet
  - The sheet normally is weak and brittle and breaks immediately into flakes.
  - These flakes need gentler treatment to break them into granules, and this can usually be achieved by screening alone.
FIG. 23-12. Schematic of dry compaction operation. Dry material is fed to and compacted by a Chilsonator, then sized to remove fines, which are recycled. The finished dry compacted granulation is ready for subsequent encapsulation or compression. Inset shows actual size of a production unit. (Courtesy of Fitzpatrick Co. © The Fitzpatrick Company, Elmhurst, IL, 1968.)
Tablet manufacturing

- Four basic requirements for successful tablet production:
  - Design
  - Equipments
  - Facility
  - Personnel
Tablet manufacturing

- Tablets are made by **compressing a formulation** containing **drug or drugs with excipients** on stamping machine called **Presses**.

- Tablet compression machines are designed with following basic components.
  - **Hopper** - for holding and feeding granulation to be compressed.
  - **Dies** that define size and shape of tablets.
  - **Punches** for compressing granulation within die.
  - **Cam tracks** for guiding movement of punches.
  - **Feeding mechanism** for moving granulation from hopper in to die.
Tablet manufacturing

- Tablet presses are classified as either
  - Single punch or
  - Multi station rotary presses.

- **Single punch** machine are called as *stamping press* as all of the compression force is applied by upper punch.

- **Multi-station presses** are termed *rotary* because the head of tablet machine that holds upper punches, dies and lower punch in press rotates.
Fig. 16  Single station press cycle.
The ultimate test of a tablet formulation and granulation process is whether the granulation can be compressed on a high-speed tablet press.

During compression, the tablet press performs the following functions:

- Filling of empty die cavity with granulation.
- Precompression of granulation (optional).
- Compression of granules.
- Ejection of the tablet from the die cavity and take-off of compressed tablet.
Tablet manufacturing

- When evaluating the compression characteristics of a particular formulation, prolonged trial runs at press speeds equal to that to be used in normal production should be tried.

- Only then are potential problems such as sticking to the punch surface, tablet hardness, capping, and weight variation detected.

- High-speed tablet compression depends on the ability of the press to interact with granulation.

- Delivery system should not change the particle size distribution.

- System should not cause segregation of coarse and fine particles, nor it should induce static charges.
Tablet manufacturing

- The die feed system must be able to fill the die cavities adequately in the short period of time that the die is passing under the feed frame.
- The smaller the tablet, the more difficult it is to get a uniform fill at high press speeds.
- For high-speed machines, induced die feed systems is necessary.
- After the die cavities are filled, the excess is removed by the feed frame to the center of the die table.
- Compression of the granulation usually occurs as a single event as the heads of the punches pass over the lower and under the upper pressure rollers.
Tablet manufacturing

- Pre compression allows the punches to penetrate the die to a preset depth, compacting the granulation to the thickness of the gap set between the punches.
- The rapidity and dwell time in between this press event occurs is determined by the speed at which the press is rotating and by the size of compression rollers.
- Larger the compressions roller, the more gradually compression force is applied and released.
Tablet manufacturing

- Slowing down the press speed or using larger compression rollers can often reduce capping in a formulation.
- The final event is ejection of compressed tablets from die cavity.
- During compression, the granularity is compacted to form tablet, bonds within compressible material must be formed which results in sticking.
- High level of lubricant or over blending can result in a soft tablet, decrease in wettability of the powder and an extension of the dissolution time.
Compression of a powder bed during tabletting

- This may be defined by a number of stages:
  - **Stage 1:** Rearrangement of the powder bed upon the application of a stress.
  - **Stage 2:** Deformation of the powders under the applied stress.
  - **Stage 3:** Bonding of the compressed powders
Compression of a powder bed during tabletting

- **Stage 1: Rearrangement of the powder bed upon the application of a stress**
  - Following the application of the initial stress, the particles in the powder bed will **undergo rearrangement to minimize the free space between particles.**
  - The extent of this rearrangement is dictated by both the size of the particles and **frictional forces** that operate between the particles.

- **Stage 2: Deformation of the powders under the applied stress**
  - During this stage the powders will **undergo deformation (elastic, plastic or fragmentation)** as a result of exposure to the applied stress.
  - The **physicochemical properties** of the powders will affect the nature of the predominant deformation type.
Compression of a powder bed during tabletting

- **Stage 3: bonding of the compressed powders.**
  - Following the application of the required stress, *interparticle bonding* occurs, resulting in the production of a tablet.

- There are two predominant bonding mechanisms in tablets prepared by direct compression:
  - Adsorption and
  - Diffusion
Defects / Problems in tablets
Problems for uncoated tablet

- The defects related to Tabletting Process:
  - Capping
  - Lamination / Laminating
  - Cracking

- The defects related to Excipients:
  - Chipping
  - Sticking / Filming
  - Picking
  - Binding

- The defect related to multiple factor:
  - Mottling

- The defect related to Machine:
  - Double impression
Problems for coated tablet

- Blistering
- Chipping
- Cratering
- Picking
- Pitting
- Blooming
- Blushing
- Color variation
- Infilling
- Orange peel/Roughness
Capping

- Capping is the term used, when the upper or lower segment of the tablet separates horizontally, either partially or completely from the main body of a tablet and comes off as a cap, during ejection from the tablet press, or during subsequent handling.

- It is due air-entrainment in the granular material

- Reason: Capping is usually due to the air–entrainment in a compact during compression, and subsequent expansion of tablet on ejection of a tablet from a die.
<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>CAUSES</th>
<th>REMEDIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Large amount of fines in the granulation</td>
<td>Remove some or all fines through 100 to 200 mesh screen</td>
</tr>
<tr>
<td>2</td>
<td>Too dry or very low moisture content (leading to loss of proper binding action)</td>
<td>Moisten the granules suitably. Add hygroscopic substance e.g.: sorbitol, methylcellulose or PEG-4000.</td>
</tr>
<tr>
<td>3</td>
<td>Not thoroughly dried granules</td>
<td>Dry the granules properly.</td>
</tr>
<tr>
<td>4</td>
<td>Insufficient amount of binder or improper binder.</td>
<td>Increasing the mount of binder</td>
</tr>
<tr>
<td>5</td>
<td>Insufficient or improper lubricant</td>
<td>Increase the amount of lubricant or change the type of lubricant.</td>
</tr>
<tr>
<td>6</td>
<td>Granular mass too cold to compress firm</td>
<td>Compress at room temperature</td>
</tr>
</tbody>
</table>
Lamination / Laminating

- **Lamination** is the separation of a tablet into two or more distinct horizontal layers.
- It is due air-entrapment in the granular material.
- **Reason:** Air–entrainment during compression and subsequent release on ejection.

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>CAUSES</th>
<th>REMEDIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Oily or waxy materials in granules</td>
<td>Modify mixing process. Add adsorbent or absorbent</td>
</tr>
<tr>
<td>2</td>
<td>Oily or waxy materials in granules</td>
<td>Use a less amount of lubricant or change the type of lubricant.</td>
</tr>
</tbody>
</table>
Chipping

- **Chipping** is defined as the breaking of tablet edges, while the tablet leaves the press or during subsequent handling and coating operations.

- It is due to rapid expansion of tablets when deep concave punches are used.


<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>CAUSES</th>
<th>REMEDIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Sticking on punch faces.</td>
<td>Dry the granules properly or increase lubrication.</td>
</tr>
<tr>
<td>2</td>
<td>Too dry granules.</td>
<td>Moisten the granules to plasticize. Add hygroscopic substances.</td>
</tr>
<tr>
<td>3</td>
<td>Too much binding causes chipping at bottom.</td>
<td>Optimize binding, or use dry binders.</td>
</tr>
</tbody>
</table>
Cracking

- Small, fine cracks observed on the upper and lower central surface of tablets, or very rarely on the sidewall are referred to as **Cracks**.

- It is due to very dry granules.

- **Reason:** It is observed as a result of rapid expansion of tablets, especially when deep concave punches are used.

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>CAUSES</th>
<th>REMEDIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Large size of granules.</td>
<td>Reduce granule size. Add fines.</td>
</tr>
<tr>
<td>2</td>
<td>Too dry granules.</td>
<td>Moisten the granules properly and add proper amount of binder.</td>
</tr>
<tr>
<td>3</td>
<td>Tablets expand.</td>
<td>Improve granulation. Add dry binders.</td>
</tr>
<tr>
<td>4</td>
<td>Granulation too cold.</td>
<td>Compress at room temperature.</td>
</tr>
</tbody>
</table>
**Sticking / Filming**

**Sticking** refers to the tablet material adhering to the die wall.

Filming is a slow form of sticking and is largely due to excess moisture in the granulation.

*Reason*: Improperly dried or improperly lubricated granules.

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>CAUSES</th>
<th>REMEDIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Granules not dried properly.</td>
<td>Dry the granules properly. Make moisture analysis to determine limits.</td>
</tr>
<tr>
<td>2</td>
<td>Too little or improper lubrication.</td>
<td>Increase or change lubricant.</td>
</tr>
<tr>
<td>3</td>
<td>Too much binder.</td>
<td>Reduce the amount of binder or use a different type of binder.</td>
</tr>
<tr>
<td>4</td>
<td>Hygroscopic granular material.</td>
<td>Modify granulation and compress under controlled humidity.</td>
</tr>
<tr>
<td>5</td>
<td>Oily or way materials</td>
<td>Modify mixing process. Add an absorbent.</td>
</tr>
<tr>
<td>6</td>
<td>Too soft or weak granules.</td>
<td>Optimize the amount of binder and granulation technique.</td>
</tr>
</tbody>
</table>
Picking

- Picking is the term used when a small amount of material from a tablet is sticking to and being removed off from the tablet-surface by a punch face.

- The problem is more prevalent on the upper punch faces than on the lower ones. The problem worsens, if tablets are repeatedly manufactured in this station of tooling because of the more and more material getting added to the already stuck material on the punch face.

- **Reason**: Picking is of particular concern when punch tips have engraving or embossing letters, as well as the granular material is improperly dried.
<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>CAUSES</th>
<th>REMEDIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Excessive moisture in granules.</td>
<td>Dry properly the granules, determine optimum limit.</td>
</tr>
<tr>
<td>2</td>
<td>Too little or improper lubrication.</td>
<td>Increase lubrication; use colloidal silica as a ‘polishing agent’, so that material does not cling to punch faces.</td>
</tr>
<tr>
<td>3</td>
<td>Low melting point substances, may soften from the heat of compression and lead to picking.</td>
<td>Add high melting-point materials. Use high melting point lubricants.</td>
</tr>
<tr>
<td>4</td>
<td>Low melting point medicament in high concentration.</td>
<td>Refrigerate granules and the entire tablet press.</td>
</tr>
<tr>
<td>5</td>
<td>Too warm granules when compressing.</td>
<td>Compress at room temperature. Cool sufficiently before compression.</td>
</tr>
<tr>
<td>6</td>
<td>Too much amount of binder.</td>
<td>Reduce the amount of binder, change the type or use dry binders.</td>
</tr>
</tbody>
</table>
Binding

- **Binding** in the die, is the term used when the tablets adhere, seize or tear in the die. A film is formed in the die and ejection of tablet is hindered. With excessive binding, the tablet sides are cracked and it may crumble apart.

- **Reason**: Binding is usually due to excessive amount of moisture in granules, lack of lubrication and/or use of worn dies.
Mottling

- **Mottling** is the term used to describe an unequal distribution of colour on a tablet, with light or dark spots standing out in an otherwise uniform surface.
- **Reason:** One cause of mottling may be a coloured drug, whose colour differs from the colour of excipients used for granulation of a tablet.
<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>CAUSES</th>
<th>REMEDIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>A coloured drug used along with colourless or white-coloured excipients.</td>
<td>Use appropriate colourants.</td>
</tr>
<tr>
<td>2</td>
<td>A dye migrates to the surface of granulation while drying.</td>
<td>Change the solvent system, Change the binder, Reduce drying temperature and Use a smaller particle size.</td>
</tr>
<tr>
<td>3</td>
<td>Improperly mixed dye, especially during ‘Direct Compression’.</td>
<td>Mix properly and reduce size if it is of a larger size to prevent segregation.</td>
</tr>
<tr>
<td>4</td>
<td>Improper mixing of a coloured binder solution.</td>
<td>Incorporate dry colour additive during powder blending step, then add fine powdered adhesives such as acacia and tragacanth and mix well and finally add granulating liquid.</td>
</tr>
</tbody>
</table>
Double impression

- **Double Impression** involves only those punches, which have a monogram or other engraving on them.
- **Reason:** is due to free rotation of the punches, which have some engraving on the punch faces.
- If the upper punch is uncontrolled, it can rotate during the short travel to the final compression stage and create a double impression.
- **CAUSES:**
  - Free rotation of either upper punch or lower punch during ejection of a tablet
- **REMEDIES:**
  - Inset a key alongside of the punch, so that it fits the punch and prevents punch rotation.
  - Newer presses have anti-turning devices, which prevent punch rotation.
Problems and remedies for tablet coating

**Blistering**: It is local detachment of film from the substrate forming blister.

**Reason**: Entrapment of gases in or underneath the film due to overheating either during spraying or at the end of the coating run.

<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Effect of temperature on the strength, elasticity and adhesion of the film.</td>
<td>Use mild drying condition.</td>
</tr>
</tbody>
</table>
Chipping

- It is a defect where the film becomes chipped and dented, usually at the edges of the tablet.
- *Reason:* Decrease in fluidizing air or speed of rotation of the drum in pan coating.

<table>
<thead>
<tr>
<th>Sr. No.</th>
<th>CAUSES</th>
<th>REMEDIES</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>High degree of attrition associated with the coating process.</td>
<td>Increase hardness of the film by increasing the molecular weight grade of polymer.</td>
</tr>
</tbody>
</table>
Cratering

- It is a defect of film coating whereby volcanic-like craters appear, exposing the tablet surface.

- *Reason:* The coating solution penetrates the surface of the tablet, often at the crown where the surface is more porous, causing localized disintegration of the core and disruption of the coating.

<table>
<thead>
<tr>
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<th>CAUSES</th>
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</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Inefficient drying.</td>
<td>Use efficient and optimum drying conditions.</td>
</tr>
<tr>
<td>2</td>
<td>Higher rate of application of coating solution.</td>
<td>Increase viscosity of coating solution to decrease spray application rate.</td>
</tr>
</tbody>
</table>
Picking

- It is defect where isolated areas of film are pulled away from the surface when the tablet sticks together and then part.
- **Reason:** Conditions similar to cratering that produces an overly wet tablet bed where adjacent tablets can stick together and then break apart.

<table>
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</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Inefficient drying.</td>
<td>Use optimum and efficient drying conditions or increase the inlet air temperature.</td>
</tr>
<tr>
<td>2</td>
<td>Higher rate of application of coating solution</td>
<td>Decrease the rate of application of coating solution by increasing viscosity of coating solution.</td>
</tr>
</tbody>
</table>
Pitting

- It is a defect whereby pits occur in the surface of a tablet core without any visible disruption of the film coating.

  *Reason*: Temperature of the tablet core is greater than the melting point of the materials used in the tablet formulation.

<table>
<thead>
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<th>CAUSES</th>
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</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Inappropriate drying (inlet air) tempt.</td>
<td>Dispensing with preheating procedures at the initiation of coating &amp; modifying the drying (inlet air) tempt. such that the tempt. of the tablet core is not greater than the m.p. of the batch of additives used.</td>
</tr>
</tbody>
</table>
Blooming

- It is a defect where coating becomes dull immediately or after prolonged storage at high temperatures.
- **Reason:** It is due to collection on the surface of low molecular weight ingredients included in the coating formulation. In most circumstances, the ingredient will be plasticizer.

<table>
<thead>
<tr>
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<th>CAUSES</th>
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</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>High conc$^n$ &amp; low molecular weight of plasticizer.</td>
<td>Decrease plasticizer conc$^n$ &amp; increase mol.wt. of plasticizer.</td>
</tr>
</tbody>
</table>
Blushing

- It is defect best described as whitish specks or haziness in the film.
- **Reason:** It is thought to be due to precipitated polymer exacerbated by the use of high coating temperature at or above the thermal gelation temperature of the polymers.

<table>
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</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>High coating temperature</td>
<td>Decrease the drying air temp.</td>
</tr>
<tr>
<td>2</td>
<td>Use of sorbitol in formulation which causes largest fall in the thermal gelation temperature of the HPC, HPMC,MC</td>
<td>Avoid use of sorbitol with HPC, HPMC,MC</td>
</tr>
</tbody>
</table>
Color variation

- A defect which involves variation in color of the film.
  - **Reason:** Alteration of the frequency and duration of appearance of tablets in the spray zone or the size/shape of the spray zone.

<table>
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<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Improper mixing, uneven spray pattern, insufficient coating, migration of soluble dyes-plasticizers and other additives during drying.</td>
<td>Go for geometric mixing, reformulation with different plasticizers and additives or use mild drying conditions.</td>
</tr>
</tbody>
</table>
Infilling

- It is defect that renders the intagliations indistinctness.
- **Reason:** Inability of foam, formed by air spraying of a polymer solution, to break. The foam droplets on the surface of the tablet breakdown readily due to attrition but the intagliations form a protected area allowing the foam to accumulate and “set”. Once the foam has accumulated to a level approaching the outer contour of the tablet surface, normal attrition can occur allowing the structure to be covered with a continuous film.

- **Causes:** Bubble or foam formation because of air spraying of a polymer solution
- **Remedies:** Add alcohol or use spray nozzle capable of finer atomization.
Orange peel / Roughness

- It is a surface defect resulting in the film being rough and nonglossy. Appearance is similar to that of an orange.
- **Reason:** Inadequate spreading of the coating solution before drying.

<table>
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</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Rapid Drying</td>
<td>Use mild drying conditions</td>
</tr>
<tr>
<td>2</td>
<td>High solution viscosity</td>
<td>Use additional solvents to decrease viscosity of solution.</td>
</tr>
</tbody>
</table>
Cracking / Splitting

- It is a defect in which the film either cracks across the crown of the tablet (cracking) or splits around the edges of the tablet (Splitting).

- **Reason:** Internal stress in the film exceeds tensile strength of the film.

---

<table>
<thead>
<tr>
<th>Sr. No.</th>
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</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Use of higher molecular weight polymers or polymeric blends.</td>
<td>Use lower mol. wt. polymers or polymeric blends. Also adjust plasticizer type and concn.</td>
</tr>
</tbody>
</table>
Evaluation of tablets

- Pharmacopoeial tests
- Official standards
- Un-official tests
- Why it is important to evaluate?