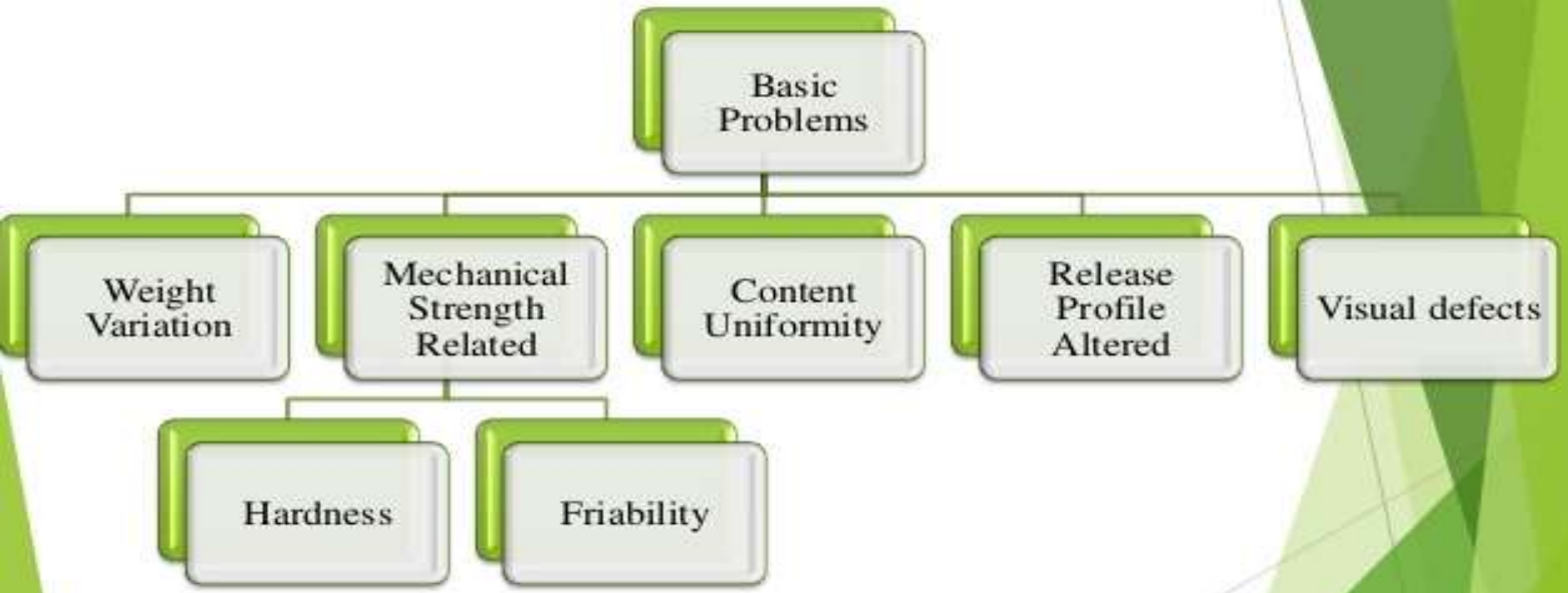
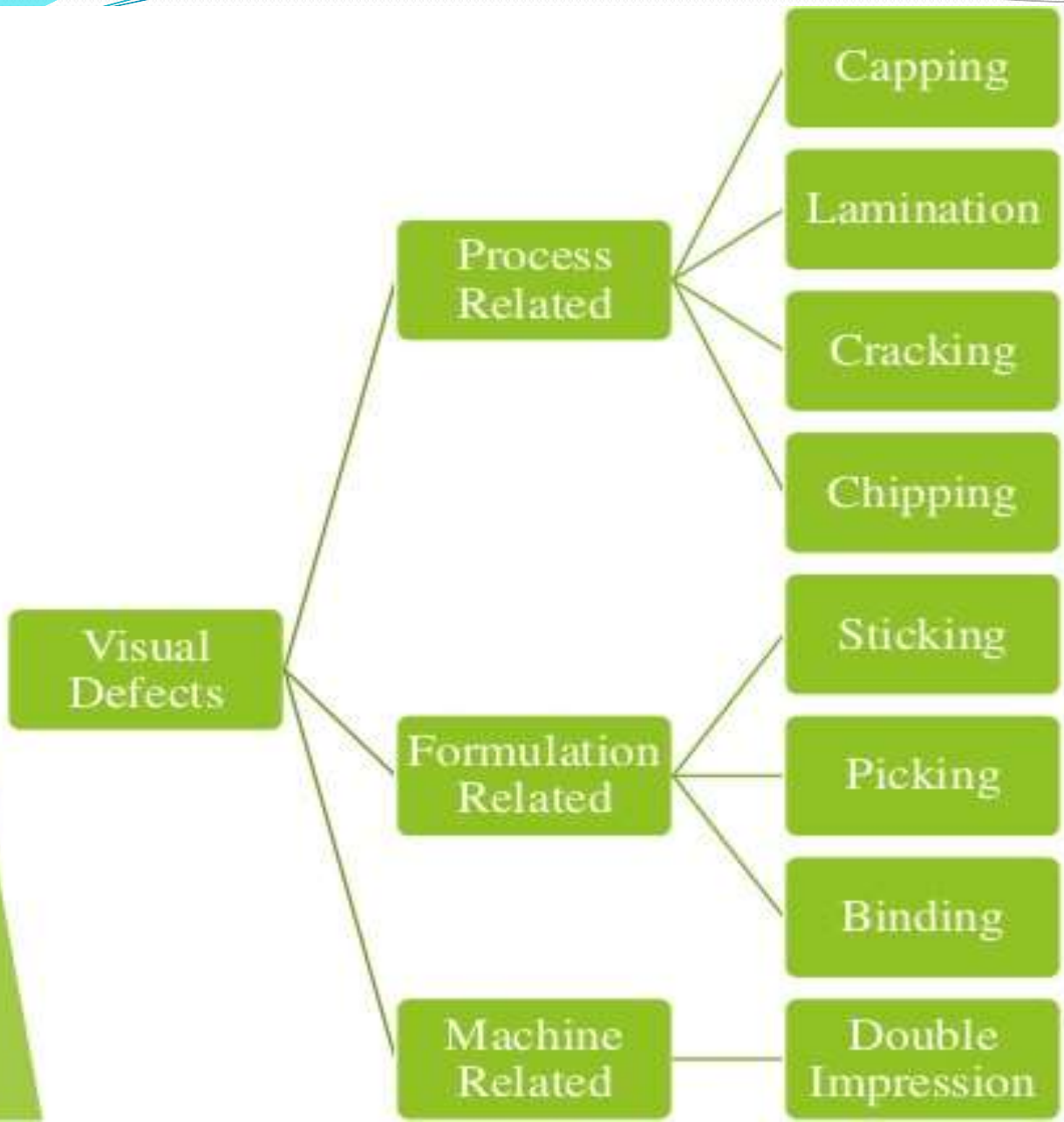
problems of tablet manufacturing


Basic Problems
Weight Variation
Mechanical Strength Related
Content Uniformity
Release Profile Altered
Visual defects
Hardness
Friability

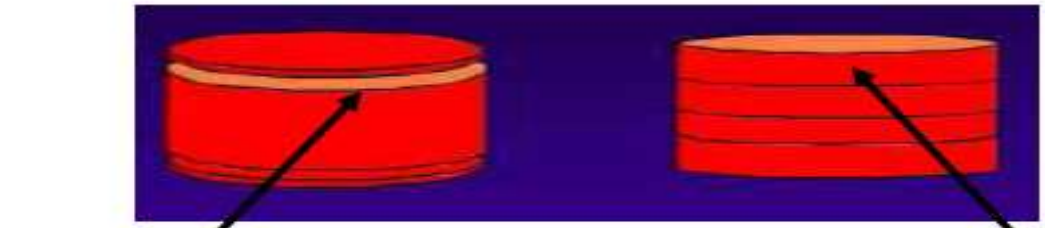
- In the normal process of developing formulations, and in the routine manufacture of tablets, various defects are observed. Sometimes, the **source** of the problem or the defect is **the formulation**, the **compression equipment**, or **a combination** of the two.
- Some defects are noticed immediately during manufacturing but others may be noticed during storage as in the case of capping.


Visual Defects
Process Related
Capping
Lamination
Cracking
Chipping
Formulation Related
Sticking
Picking
Binding
Machine Related
Double Impression

CAPPING AND LAMINATION

- **Capping** is defined as the partial or complete separation of the top or bottom crowns of a tablet from the main body of the tablet.
- **Lamination** is the separation of a tablet into two or more distinct layers.
- These processing problems are readily apparent **immediately** after compression or may occur hours or even days later.
- Subjecting tablets to the friability test is the quickest way of revealing such problems.

CAPPING AND LAMINATION



Capping

Lamination

Good tablet

Causes

- **Air entrapment** . Due to the air–entrapment in a compact during compression, and subsequent expansion of tablet on ejection of a tablet from a die.

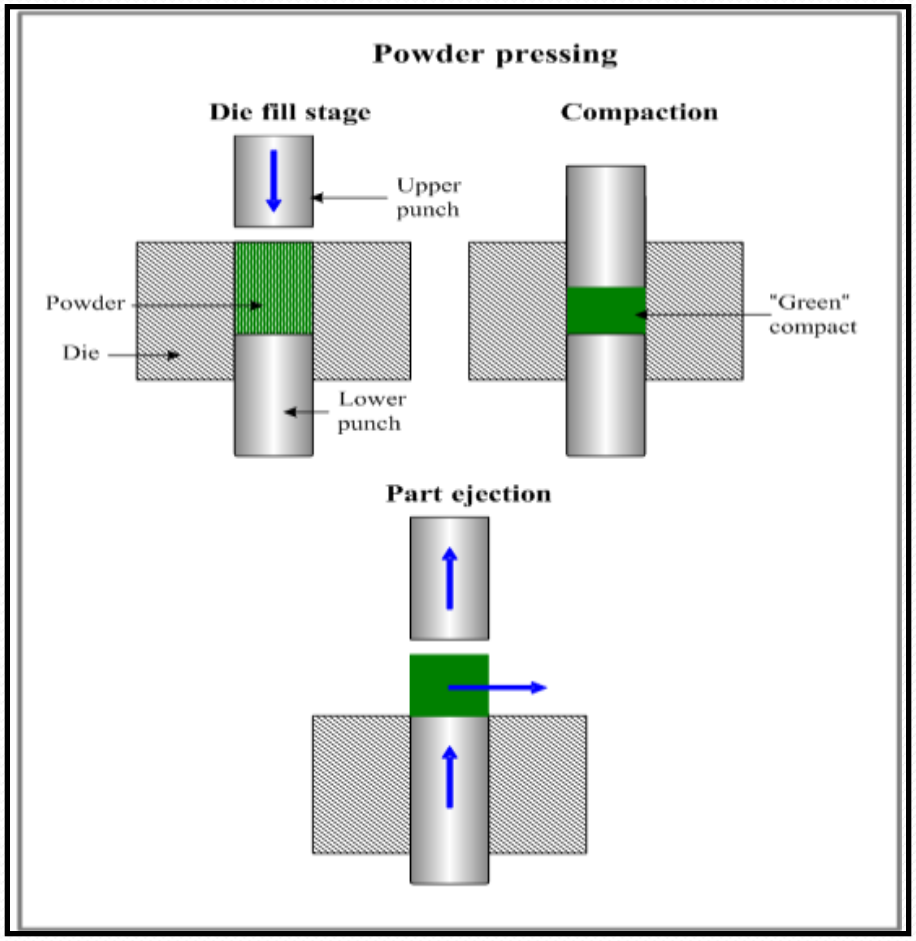
- capping and lamination may also be encountered in **direct compression**
- **Tablet tooling** (punch worn tips, deep concave punch) can cause capping .
- Incorrect setup at the press.

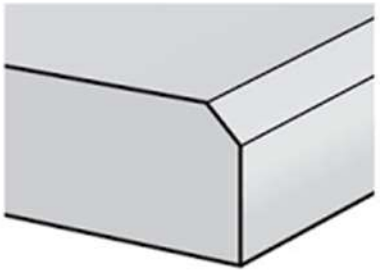
CORRECTIVE ACTIONS (Formulation)

Sr. No.	CAUSES	REMEDIES
1.	Large amount of fines in the granulation	Remove some or all fines through 100 to 200 mesh screen
2.	Too dry or very low moisture content (leading to loss of proper binding action).	Moisten the granules suitably. Add hygroscopic substance e.g.: Sorbitol, Methylcellulose or PEG-4000.
3.	Not thoroughly dried granules.	Dry the granules properly.
4.	Insufficient amount of binder or improper binder.	Increasing the amount of binder OR Adding dry binder such as pre-gelatinized Starch, Gum acacia, powdered Sorbitol, PVP, hydrophilic Silica or powdered Sugar.
5.	Insufficient or improper lubricant.	Increase the amount of lubricant or change the type of lubricant.
6.	Granular mass too cold to compress firm.	Compress at room temperature.

Machine

Sr. No.	CAUSES	REMEDIES
1.	Poorly finished dies	Polish dies properly. Investigate other steels or other materials.
2.	Deep concave punches or beveled-edge faces of punches.	Use flat punches.
3.	Lower punch remains below the face of die during ejection.	Make proper setting of lower punch during ejection.
4.	Incorrect adjustment of sweep-off blade.	Adjust sweep-off blade correctly to facilitate proper ejection.
5.	High turret speed.	Reduce speed of turret (Increase dwell time).


Powder pressing
Die fill stage
Compaction
Upper punch
Powder
Die
Lower punch
"Green" compact
Part ejection



Bevel

Chipping : is breaking of the edge of tablet during compression.

Reason:

Incorrect machine settings.

Chipping

The Causes and Remedies of Chipping related to 'Formulation'

Sr. No.	CAUSES	REMEDIES
1.	Sticking on punch faces	Dry the granules properly or increase lubrication.
2.	Too dry granules.	Moisten the granules to plasticize. Add hygroscopic substances.
3.	Too much binding causes chipping at bottom.	Optimize binding, or use dry binders.

- Cracking: small, fine cracks observed in the upper and lower central surface of tablets or very rarely on the side wall are referred to as cracks .
- *Reason:*
  - It is observed as a result of rapid expansion of tablets, especially when deep concave punches are used.

The Causes and Remedies of Cracking related to ‘Formulation’

Sr. No.	CAUSES	REMEDIES
1.	Large size of granules.	Reduce granule size. Add fines.
2.	Too dry granules.	Moisten the granules properly and add proper amount of binder.
3.	Tablets expand.	Improve granulation. Add dry binders.
4.	Granulation too cold.	Compress at room temperature.

POP QUIZ

- Capping is prevented by using ------- face punches

(a) Flat (b) concave

(c) convex (d) worn

PICKING AND STICKING

- **Picking** refers to term used when small amount of surface material of tablet stick to and being removed off from the tablets surface by a punch face.
- It is of particular concern when **punch tips have engraving or embossing**. **Small enclosed letter** (A,B,O,Q) are difficult to manufacturing cleanly
- Tablet materials adhering to punches can accumulate to the point of obliterating the tip design.
- **Sticking** refers to a tablet material adhering to the die wall.
- It results in the buildup of material on punch faces.

- **Low melting point substances**, either active ingredients or additives such as stearic acid or PEG, may soften sufficiently from the heat of compression.
- **Excessive moisture** may be responsible for sticking and further drying of granulation is then required.

Remedy

- **Lettering** should be designed as **large** as possible particularly on punches with small diameter.
- The tablets can perhaps be reformulated to larger size.
- **Plating punch face with chromium** is a method of producing a smooth , non adherent face.
- **Colloidal silica** added to the formula act as a **polishing agent** and makes the punch faces too smooth so that material does not sticking to them.
- **Lubricants** required to overcome friction between tablet and die wall during ejection.

BINDING

Binding in the die is the term used when tablet stick to the die and does not eject properly.

Tablets **adhere, seize and tear** in the die. A film is formed in the die and tablet ejection is hindered and become difficult and accompanied by characteristic noise.

The edge of tablet becomes rough , tablet side cracks and it may be crumble.

Causes :

- Poor lubrication of granules
- Under dried granules
- Dirty or worn out dies
- Fine powder from granules seep outward and forms thick layer on die which hinders free movement of punches

MOTTLING

- Mottling is unequal distribution of color on a tablet, with light or dark areas standing out in an otherwise uniform surface.

Causes and corrective actions:

- **Drug whose color differs from the tablet excipients or a drug whose degradation products are colored**.
- Use of colorants
- **Migration of dyes to the surface of granulation during drying**
- Change the solvent system (binding system)
- Reduce the drying temperature
- Insoluble lake
- **The use of colorant in direct compression formulations can lead to mottling if dye is not well dispersed or if its size too large**
- Mix properly and reduce size to a small particle size if too large

POP QUIZ

- Match the following and find out the correct combination

1. Capping (A) Separation of a tablet into 2 or more layers

2. Lamination (B) Unequal distribution of color on a tablet

3. Mottling (C) Separation of top/bottom crowns of a tablet from the main body

4. Sticking (D) Adherence of tablet material to the die wall

DOUBLE IMPRESSION

- This problem is encountered with punches that have a **monogram** or other **engraving** on them.
- If the letters of tablet are impressed twice then they are known as double impression

- At the moment of compression, the tablet receives the imprint of the punch.
- The lower punch freely drops and travels uncontrolled for a short distance before riding up the ejection cam to push the tablet out of the die
- Now during this free travel, the punch rotates and at this point, the punch may make a new impression on the bottom of the tablet, resulting in 'double impression'.

Double impression

The Causes And Remedies	
Causes	**Remedies**
Free rotation of either upper punch or lower punch during ejection of a tablet.	-Use keying in tooling, i.e. 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.

WEIGHT VARIATION

Weight of tablet determined by **amount of granulation in die** prior to compression. Therefore, anything that alter die-filling alter tablet weight.

Causes and remedies

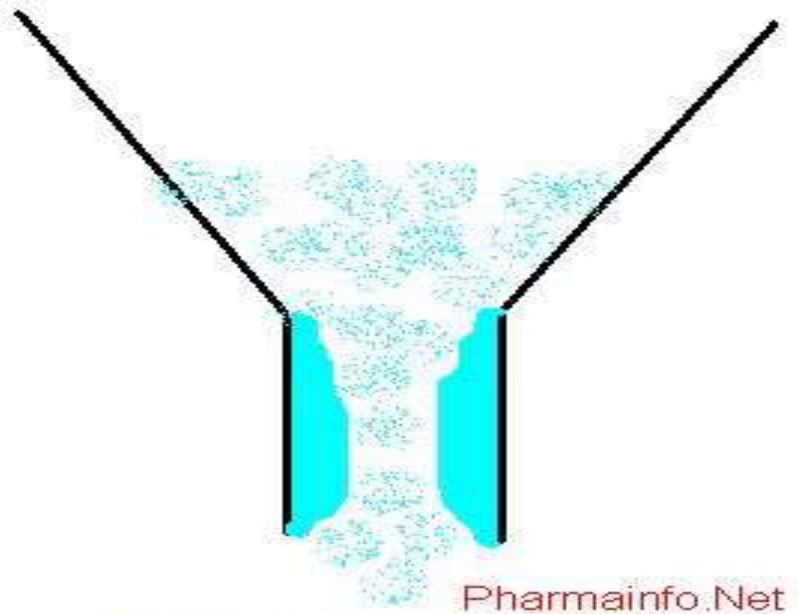
- **Granular size and size distribution before compression:**

Variation in the ratio of small and large granules influence how the void spaces between particles are filled. Thus may change the weight of fill in each die.

- **Poor flow through the Feed frame**

As particle move under the force of gravity through progressively smaller openings, they are subjected to uneven pressures from mass above and alongside. Depending on geometry of the hopper, this situation may give rise to one or another of two cause for poor flow (arching) or (bridging of particles that blocks flow) and (rat-holing) (an empty tunnel over the orifice due to core-flow).

- **Particles size should be optimum** for good flowing of granules from hopper to die.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RAT-HOLING

➢ Poor mixing

Sometimes lubricants and glidants are not properly distributed. Then the flow of particles impaired and granules do not move efficiently into die.

- **Good lubricant** should be used. **Uniform mixing** of the materials can overcome this defect
- Lubricant & glidants should be added in mixing time.

➢ Punch variation

When lower punches of unequal lengths. The difference may be only a few thousandth of an inch. The fill in each die varies because the fill is volumetric.

- **Good punch and die which has uniform dimensions** can control weight variation.

- Machines built to compress tablets consist of:

- 1- Hopper: for holding granulations for compressing.
- 2- Feed frame: for distributing the materials into the dies.
- 3- Dies: for controlling the size and the shape of the tablet.
- 4- Punches: for compressing the granulations within the dies.


Big hopper for holding large powder!!

HARDNESS VARIATION

- Hardness variation is a problem that has the same causes as weight variation.
- Tablet which is **very hard** is not acceptable as well as **very soft** because this type of tablet would be broken rapidly or slowly but not in consideration time.

Causes and remedies

- Hardness depend on weight of material ⟶ **weight should be taken carefully.**
- **The space between upper & lower punches** at moment of compression . If the volume of material or distance between punches varies leading to in consist hardness.

THANK YOU