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REVIEW ARTICLE

MANUFACTURING DEFECTS OF TABLETS - A REVIEW

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ABSTRACT

Tablet defects can come from any of the unit operation upstream and from the tablet press. The raw materials may be of poor quality or do not meet specification, causing excessive fines that lead to a host of defects. The formulation may be the source of defects if the material do not compress well or the processing step specified within the formulation fail to produce a powder a good flow, compressibility, and ejection properties. The processing and granulation of powder is often the source of defect. Every product behaves differently on a tablet press, even if it's the same product run on a different day. The variation often stems from changes in the properties of the raw materials—active ingredients and excipients- from batch to batch. Naturally, the goal is to minimize these changes. Tablet press operators, however, don't have any control over formulation and granulation. Tablet specifications are tight, and the list of possible defects is long: Variable weight, sticking, picking, capping, lamination, variable hardness, among others. This article focuses on these variations. It pinpoints the possible causes of these defects and offers advice on preventing and fixing the source of the problems.

Key words: capping, mixing, granules, punches, compression, cracking

INTRODUCTION

An ideal tablet should be free from any visual defect or functional defect. The advancements and innovations in tablet manufacture have not decreased the problems, often encountered in the production, instead have increased the problems, mainly because of the complexities of tablet presses; and/or the greater demands of quality. An industrial pharmacist usually encounters number of problems during manufacturing. Majority of visual defects are due to inadequate fines or inadequate moisture in the granules ready for compression or due to faulty machine setting. Functional defects are due to faulty formulation. Solving many of the manufacturing problems requires an in-depth knowledge of granulation processing and tablet presses, and is acquired only through an exhaustive study and a rich experience.

Here, we will discuss the imperfections found in tablets along-with their causes and related remedies. The imperfections are known as: 'Visual Defects' and they are either related to imperfections in any one or more of the factors.²

Tablet processing problems can be due to the problem in the formulation or in the compression equipment, or both of them. Thus we can classify the problems into following types:

The defects related to Tableting Process

i) Capping: It is partial or complete separation of the top or bottom of tablet due air-entrapment in the granular material.

ii) Lamination: It is separation of tablet into two or more layers due to air-entrapment in the granular material.

iii) Cracking: It is due to rapid expansion of tablets when deep concave punches are used.^{2, 3}

The defects related to Excipient

iv) Chipping: It is due to very dry granules.

v) Sticking: It is the adhesion of granulation material to the die wall

vi) Picking: It is the removal of material from the surface of tablet and its adherence to the face of punch.

vii) Binding: These problems (v, vi, vii) are due to more amount of binder in the granules or wet granules.

The defect related to more than one factor

viii) Mottling: It is either due to any one or more of these factors: Due to a colored drug, which has different color than the rest of the granular material (Excipient- related); improper mixing of granular material (Process-related); dirt in the granular material or on punch faces; oil spots by using oily lubricant.

The defect related to Machine

ix) Double Impression: It is due to free rotation of the punches, which have some engraving on the punch faces.

Further, in this section, each problem is described along-with its causes and remedies which may be related to either of formulation (granulation) or of machine (dies, punches and entire tablet press).

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.

Reason: Capping is usually due to the air-entrapment in a compact during compression, and subsequent expansion of tablet on ejection of a tablet from a die.^{6,7}

The Causes and Remedies of Capping Related To 'Formulation' (Granulation)

Causes

- I. Large amount of fines in the granulation
- II. Too dry or very low moisture content (leading to loss of proper binding action).
- III. Not thoroughly dried granules.
- IV. Insufficient amount of binder or improper binder.
- V. Insufficient or improper lubricant.
- VI. Granular mass too cold.

Remedies

- I. Remove some or all fines through 100 to 200 mesh screen.
- II. Moisten the granules suitably. Add hygroscopic substance e.g.: sorbitol, methyl- cellulose or PEG-4000.
- III. Dry the granules properly.
- IV. Increasing the amount of binder.
- V. Adding dry binder such as pre-gelatinized starch, gum acacia, powdered sorbitol, PVP, hydrophilic silica or powdered sugar.
- VI. Increase the amount of lubricant or change the type of lubricant.
- VII. Compress at room temperature.

The Causes and Remedies Of Capping Related To 'Machine' (Dies, Punches And Tablet Press)

Causes

- I. Poorly finished dies
- II. Deep concave punches or beveled-edge faces of punches.
- III. Lower punch remains below the face of die during ejection.
- IV. Incorrect adjustment of sweep-off blade.
- V. High turret speed

Remedies

- I. Polish dies properly. Investigate other steels or other materials.
- II. Use flat punches.
- III. Make proper setting of lower punch during ejection.
- IV. Adjust sweep-off blade correctly to facilitate proper ejection.
- V. Reduce speed of turret (Increase dwell time).

LAMINATION

'Lamination' is the separation of a tablet into two or more distinct horizontal layers.

Reason: Air-entrapment during compression and subsequent release on ejection.

The condition is exaggerated by higher speed of turret.⁸

The Causes and Remedies of Lamination Related To Formulation (Granulation)

Causes

- I. Oily or waxy materials in granules.
- II. Too much of hydrophobic lubricant.
- III. Magnesium-stearate.

Remedies

- I. Modify mixing process. Add adsorbent or absorbent.
- II. Use a less amount of lubricant or change the type of lubricant.

The Causes And Remedies Of Lamination Related To 'Machine' (Dies, Punches And Tablet Press)

Causes

- I. Rapid relaxation of the peripheral regions of a tablet, on ejection from a die.
- II. Rapid decompression

Remedies

- I. Use tapered dies, i.e. upper part of the die bore has an outward taper of 3° to 5°.
- II. Use pre-compression step. Reduce turret speed and reduce the final compression pressure.

CHIPPING

'Chipping' is defined as the breaking of tablet edges, while the tablet leaves the press or during subsequent handling and coating operations. Reason: Incorrect machine settings, specially mis-set ejection take-off.⁶

The Causes And Remedies Of Chipping Related To Formulation (Granulation)

Causes

- I. Sticking on punch faces
- II. Too dry granules.
- III. Too much binding causes chipping at bottom.

Remedies

- I. Dry the granules properly or increase lubrication.
 - II. Moisten the granules to plasticize. Add hygroscopic substances.
- Optimize binding, or use dry binders.

The Causes And Remedies Of Chipping Related To 'Machine' (Dies, Punches And Tablet Press)

Causes

- I. Groove of die worn at compression point.
- II. Barreled die (center of the die wider than ends)
- III. Edge of punch face turned inside/inward.
- IV. Concavity too deep to compress properly.

Remedies

- I. Polish to open end, reverse or replace the die.
- II. Polish the die to make it cylindrical
- III. Polish the punch edges
- IV. Reduce concavity of punch faces. Use flat punches.

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'. Reason: It is observed as a result of rapid expansion of tablets, especially when deep concave punches are used.⁹

The Causes And Remedies Of Cracking Related To Formulation (Granulation)

Causes

- I. Large size of granules.
- II. Too dry granules.
- III. Tablets expand.
- IV. Granulation too cold.

Remedies

- I. Reduce granule size. Add fines.
- II. Moisten the granules properly and add proper amount of binder.
- III. Improve granulation. Add dry binders.
- IV. Compress at room temperature.

The Causes And Remedies Of Cracking Related To Machine (Dies, Punches And Tablet Press)

Causes

- I. Tablet expands on ejection due to air entrapment
- II. Deep concavities cause cracking while removing tablets

Remedies

- I. Use tapered die.
- II. Use special take-off.

STICKING

'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.⁴

The Causes And Remedies Of Sticking Related To Formulation (Granulation)

Causes

- I. Granules not dried properly.
- II. Too little or improper lubrication.
- III. Too much binder
- IV. Hygroscopic granular material.
- V. Oily or waxy materials
- VI. Too soft or weak granules.

Remedies

- I. Dry the granules properly. Make moisture analysis to determine limits.
- II. Increase or change lubricant.
- III. Reduce the amount of binder or use a different type of binder.
- IV. Modify granulation and compress under controlled humidity.
- V. Modify mixing process. Add an absorbent.
- VI. Optimize the amount of binder and granulation technique.

The Causes And Remedies Of Sticking Related To Machine (Dies, Punches And Tablet Press)

Causes

- I. Concavity too deep for granulation.
- II. Too little pressure.
- III. Compressing too fast.

Remedies

- I. Reduce concavity to optimum.
- II. Increase pressure.
- III. Reduce speed.

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.⁴

The Causes and Remedies Of Picking Related To Formulation (Granulation)

Causes

- I. Excessive moisture in granules.
- II. Too little or improper lubrication.
- III. Low melting point substances, may soften from the heat of compression and lead to picking.
- IV. Low melting point medicament in high concentration.
- V. Too warm granules when compressing.
- VI. Too much amount of binder.

Remedies

- I. Dry properly the granules, determine optimum limit.
- II. Increase lubrication; use colloidal silica as a 'polishing agent', so that material does not cling to punch faces.
- III. Add high melting-point materials. Use high melting point lubricants.
- IV. Refrigerate granules and the entire tablet press.
- V. Compress at room temperature. Cool sufficiently before compression.
- VI. Reduce the amount of binder, change the type or use dry binders.

The Causes And Remedies Of Picking Related To Machine (Dies, Punches And Tablet Press)

Causes

- I. Rough or scratched punch faces.
- II. Bevels or dividing lines too deep.
- III. Pressure applied is not enough; too soft tablets.

Remedies

- I. Polish faces to high luster.
- II. Design lettering as large as possible.
- III. Plate the punch faces with chromium to produce a smooth and non-adherent face.
- IV. Reduce depths and sharpness.
- V. Increase pressure to optimum.

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.^{2,3}

The Causes And Remedies Of Binding Related To Formulation (Granulation)

Causes

- I. Too moist granules and extrudes around lower punch.
- II. Insufficient or improper lubricant.
- III. Too coarse granules.
- IV. Too hard granules for the lubricant to be effective.
- V. Granular material very abrasive and cutting into dies.
- VI. Granular material too warm.
- VII. sticks to the die.

Remedies

- I. Dry the granules properly.
- II. Increase the amount of lubricant or use a more effective lubricant.
- III. Reduce granular size, add more fines, and increase the quantity of lubricant.
- IV. Modify granulation. Reduce granular size.
- V. If coarse granules, reduce its size.
- VI. Use wear-resistant dies.
- VII. Reduce temperature.
- VIII. Increase clearance if it is extruding.

The Causes And Remedies Of Binding Related To Machine (Dies, Punches And Tablet Press)

Causes

- I. Poorly finished dies.
- II. Rough dies due to abrasion, corrosion.
- III. Undersized dies. Too little clearance.
- IV. Too much pressure in the tablet press.

Remedies

- I. Polish the dies properly.
- II. Investigate other steels or other materials or modify granulation.
- III. Rework to proper size. Increase clearance.
- IV. Reduce pressure. Or Modify granulation.

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.²

The Causes And Remedies Of Mottling

Causes

- I. A coloured drug used along with colourless or white-coloured excipients.
- II. A dye migrates to the surface of granulation while drying.
- III. Improperly mixed dye, especially during 'Direct Compression'.
- IV. Improper mixing of a coloured binder solution.

Remedies

- I. Use appropriate colourants.
- II. Change the solvent system, Change the binder, Reduce drying temperature and Use a smaller particle size.
- III. Mix properly and reduce size if it is of a larger size to prevent segregation.
- IV. 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.

DOUBLE IMPRESSION

'Double Impression' involves only those punches, which have a monogram or other engraving on them. Reason: At the moment of compression, the tablet receives the imprint of the punch. Now, on some machines, 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'.³

Cause

Free rotation of either upper punch or lower punch during ejection of a tablet.

Remedies

- I. Use keying in tooling, i.e. inset a key alongside of the punch, so that it fits the punch and prevents punch rotation.
- II. Newer presses have anti-turning devices, which prevent punch rotation.

Tablet weight: Sources of variation

The tablet weights are mainly affected by following reasons :

Product variation: This type of variation can be due to inconsistent powder density and particle size distribution. Density can change on the press, often because of overfilling of the die and re-circulation of the powder on the tablet press, whereas particle size distribution may change when the product becomes unblended during transfer or because of static electricity. This may also change because the product cannot withstand the handling

and the mechanical stress it undergoes before reaching the tablet press.

Machine condition: The problems caused by a tablet press that is poorly prepared or operated are legion. The up and down motion under load on a new die table should be within 0.003 inch of the setting. Care must be taken to ensure that the pressure rolls and cams are in very good condition.

Tooling condition: The punch working length should be taken in consideration. Working length is an important factor in how punches affect tablet weight. New tools are made to a tolerance of one-thousandth of an inch, the length of each punch is correct and identical.

Powder flow and feed-rates: Various defects are related to powder flow and feed-rates stem, therefore powder flow and feed-rates should be taken in account while manufacturing of tablets.

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.⁹

The Cause and Remedy Of Blistering**Cause**

Effect of temperature on the strength, elasticity and adhesion of the film.

Remedy

Use mild drying condition.

CRATERING

It is defect of film coating whereby volcanic-like craters appears exposing the tablet surface.⁹

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.

The Causes And Remedies Of Cratering**Causes**

- I. Inefficient drying.
- II. Higher rate of application of coating solution.

Remedies

- I. Use efficient and optimum drying conditions.
- II. Increase viscosity of coating solution to decrease spray application rate.

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.

The Causes And Remedies Of Picking

Cause

- I. Inefficient drying.
- II. Higher rate of application of coating solution.

Remedy

- I. Use optimum and efficient drying conditions or increase the inlet air temperature.
- II. Decrease the rate of application of coating solution by increasing viscosity of coating solution.

PITTING

It is 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.¹⁰

The Cause And Remedy Of Pitting

Cause

Inappropriate drying (inlet air) temperature.

Remedy

Dispensing with preheating procedures at the initiation of coating and modifying the drying (inlet air) temperature such that the temperature of the tablet core is not greater than the melting point of the batch of additives used.

BLOOMING

It is 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.⁹

The Cause And Remedy Of Blooming

Cause

High concentration and low molecular weight of plasticizer.

Remedy

Decrease plasticizer concentration and increase molecular weight of plasticizer.

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.⁷

The Causes And Remedies Of Blushing

Causes

- I. High coating temperature.
- II. Use of sorbitol in formulation which causes largest fall in the thermal gelation temperature of the Hydroxy Propyl Cellulose, Hydroxy Propyl Methyl Cellulose, Methyl Cellulose and Cellulose ethers.

Remedies

- I. Decrease the drying air temperature.
- II. Avoid use of sorbitol with Hydroxy Propyl Cellulose, Hydroxy Propyl Methyl Cellulose, Methyl Cellulose and Cellulose ethers.

Colour variation

A defect which involves variation in colour 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.⁸

The Cause And Remedy Of Colour Variation

Cause

Improper mixing, uneven spray pattern, insufficient coating, migration of soluble dyes-plasticizers and other additives during drying.

Remedy

Go for geometric mixing, reformulation with different plasticizers and additives or use mild drying conditions.

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.⁶

The Cause And Remedy Of Infilling

Cause

Bubble or foam formation because of air spraying of a polymer solution.

Remedy

Add alcohol or use spray nozzle capable of finer atomization.

ORANGE PEEL/ROUGHNESS

It is 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.⁶

The Causes and Remedies Of Orange Peel/Roughness

Causes

- I. Rapid Drying
- II. High solution viscosity

Remedies

- I. Use mild drying conditions.
- II. Use additional solvents to decrease viscosity of solution.

Cracking/Splitting

It is 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.⁴

The Cause of Cracking/Splitting

Cause

- I. Use of higher molecular weight polymers or polymeric blends.
- II. Use lower molecular weight polymers or polymeric blends. Also adjust plasticizer type and concentration.

BRIDGING

This occurs when the coating fills in the lettering or logo on the tablet and is typically caused by improper application of the solution, poor design of the tablet embossing, high coating viscosity, high percentage of solids in the solution, or improper atomization pressure. During drying, the film may shrink and pull away from the

sharp corners of an intagliation or bisect, resulting in a "bridging" of the surface. This defect can be so severe that the monogram or bisect is completely obscured. Remedy: Increasing the plasticizer content or changing the plasticizer can decrease the incidence of bridging.¹⁰

CONCLUSION

Tablets are the most common and frequently used among oral dosage forms. This is due to its relative low cost and ease of administration. Defects in the tablets can arise during manufacturing processes, storage or transport. These visual defects can reduce the acceptability by the users and effectiveness of the product. In this review defects, causes and measures to overcome these defects have been discussed and that the same could be minimized and prevented. The focus of this discussion was to establish ways to resolve common defects at the tablet press, and to identify the root cause of each and finally resolve the defect before it reaches the tablet press.

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