IJCSPUB.ORG ISSN : 2250-1770

INTERNATIONAL JOURNAL OF CURRENT SCIENCE (IJCSPUB)

IJCS PUBLICATION (IJCSPUB.ORG) An International Open Access, Peer-reviewed, Refereed Journal

MANUFACTURING DEFECTS OF TABLET

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Abstract:

Tablet manufacturing defects can be due to a variety of factors, including off-spec raw materials, formulation issues, and processing and granulation issues. These imperfections can cause weight differences, blocking, sealing, and lamination issues. While the tablet press operator has no control over formulation and granulation, it is important to minimize batch-to-batch variation in raw material properties. By identifying possible causes of these defects and taking steps to prevent and correct the root cause of the problem, manufacturers can help ensure that each batch of tablets is consistent and meets specifications.

Keywords: Capping, Lamination, cracking, binding, sticking, punches, tablet, double impression.

Introduction:

Tablets are defined as solid pharmaceutical dosage forms that are formed either through compression or moulding techniques and typically contain medicinal material with acceptable diluents (1). Because similar coating sub caste abnormalities, internal crevices, and delamination can occur in a drug tablet, quality assurance monitoring is pivotal in the pharmaceutical sector (2). During production, an artificial druggist generally runs into a number of issues. The maturity of aesthetic excrescences is caused by either inadequate forfeitures or humidity in the grains that are ready for contraction or by indecorous machine settings. Ineffective expression is the cause of functional problems. We'll talk about tablet excreencies in this composition, along with their causes and remedial conduct (3).A tablet is an oral dosage form (oral solid dosage form, or osd) or solid unit dosage form of a drug. It is a mixture of the active ingredient and excipients, usually in powder form, from which the powder is compressed or compacted into a fixed dose (4). An ideal tablet should be free from any visual or functional disfigurement. The advancements and inventions in tablet manufacture haven't dropped the problems frequently encountered in the product; rather, they have increased the problems substantially because of the complications of tablet presses and/or the lesser demands on quality. An artificial druggist generally encounters a number of problems during manufacturing (5). Tablet specifications are tight, and the list of possible blights is long: variable weight, sticking, blackening, locking, lamination, variable hardness, etc. This composition focuses on these variants. It identifies possible causes of these blights and provides recommendations on how to help them and how to address the root cause of the problem (6).

The defects related to tableting process (5):

1. Capping: This is due to partial or complete separation of the top or bottom of the tablet due to air pockets in the grainy material.
2. Lamination: this is the separation of the tablet into two or more layers due to the addition of air in the grainy material.

3. Cracking: this is due to the rapid-fire expansion of the tablet when the hollow punch is used.

The defects related to excipient:

4. Chipping: this is due to very dry particles.
5. Sticking: this is the adhesion of the particulate material to the mould wall.
6. Picking: this is the removal of material from the tablet surface and its adhesion to the punch surface.
7. Binding: these problems (5, 6, 7) are due to a large amount of binder in the pellet or in the wet pellet.

The defect related to more than one factor:

8. Mottling: it may be caused by one or more of the following: a colored drug that is different in color from the rest of the granular material (excipient-related); improper granular material mixing (process-related); dirt in the granular material or on punch faces; or oil spots from the use of oily lubricant.

The defect related to machine:

9. Double impression: this is due to the free rotation of the stamp and some engravings on the surface of the stamp. Additionally, this section describes each problem that may be associated with either formulation (granulation), along with its cause and remedy. Or from the machine (die, punch, and the whole tablet press).

Capping:

In addition, optimizing the formulation of the tablet and ensuring proper lubrication can also help reduce capping. Choosing the right processing equipment and tools, such as using a tablet press with a proper filling system and carefully maintaining the tooling, can also help prevent capping. Moreover, adjusting the compression force and the speed of the tablet press can also influence capping. It is essential to perform regular maintenance checks and clean the equipment to avoid any contamination, which can lead to capping. Furthermore, selecting suitable excipients, such as binders and disintegrate, can enhance the compression behavior of tablets and minimize capping. Ensuring that the tablet is packed and stored appropriately can also help prevent capping (1.1). Overall, preventing capping is a complex process that requires careful consideration of various factors. Proper formulation, processing, and equipment maintenance are crucial to minimizing capping and producing high-quality tablets (1). Capping occurs when the cap or top of the tablet separates from the solid tablet's body. Capping as a result of poor formulation and processing techniques (3).

Fig. 1- Capping defect in tablet (7)

Causes (8):

1. Excessive compression force or speed of tablet pressing.
2. Inconsistent flow rate of granulation.
3. Inappropriate selection of excipients.
4. High temperature during compression.
5. Uneven distribution of particles in the granulation.

6. Air entrapment during compression.
7. Inadequate consolidation of granulation during compression.
8. Inconsistent thickness of tablet punch faces.
9. Poor mixing of ingredients in the granulation.
10. Improper filling of granulation in the tooling.
11. Ageing of the granulation.
12. Inadequate lubrication of tooling.
13. Variations in ambient temperature and humidity.
14. Improper adjustment of tablet press settings.
15. Non-uniform particle size distribution.
16. Improper blending of ingredients.
17. Inadequate granulation drying time.
18. Poor powder flow characteristics.
19. Air pockets within granulation.

Remedies (8):

1. To increase the lubrication of the tooling.
2. To monitor and control the temperature and humidity in the production area.
3. To optimize the tablet press settings according to the characteristics of the granulation.
4. To improve the particle size distribution through milling or sieving.
5. To ensure proper blending of ingredients through sufficient mixing time and methods.
6. To increase the drying time of granulation if necessary.
7. To improve powder flow characteristics through the addition of flow agents or other excipients.
8. To minimize air pockets within granulation through proper mixing and filling techniques.

Lamination:

When making pharmaceutical tablets, lamination is a frequent industrial issue. It relates to the tablet failing in one or more planes that are perpendicular to the surface and pass through the tablet band. However, there are various types of lamination, and this work suggests a classification of the various situations. A multiple fracture brought on by air entrapment falls under Type 1. Because of the shear tensions that form as the tablet comes out of the die, type 2 happens. Type 3 only affects convex tablets and is brought on by a tensile tension that forms in the tablet's center at the conclusion of unloading and spreads further towards the band. Experimental research on one example of each kind was conducted to test three industrial-level approaches that have traditionally been used: delaying the press, utilizing a precompression, and using a tapered die. Results indicate that lamination type 1 can be minimized by slowing down the press or utilizing a recompression, consistent with the mechanisms that have been postulated. Only the tapered die solution prevented lamination for type 2. Lamination type 3 was not entirely resolved by any of the remedies. However, the use of a tapered die lessened the issue's severity by preventing the crack from spreading to the surface (9).

If observable fissures are seen on the ejected tablet, lamination caused by air entrapment is easily recognized, signaling the need for processing parameter correction or reformulation. However, the identification of such an issue can take longer if some borderline formulations internalize the flaws. Then, concealed flaws may result in an inaccurate description of inherent material characteristics, such as compressibility, tablet ability, and compatibility, which guide tablet formulation design. As a result, a quick and accurate method for early diagnosis of air entrapment problems is required to inform the efficient design of robust tablet formulations (10).

Fig. 2- Lamination defect in tablet (7)

Causes (11):

1. Poor compression force applied during tablet production.
2. Inadequate granule flow properties.
3. Insufficiently adjusting the tablet press settings.
4. Use of poor-quality excipients.
5. Deterioration or breakage of the tooling.
6. Inadequate tablet press cleaning and maintenance.
7. Presence of moisture in the granulation.

Remedies (11):

1. Reduce or eliminate the use of magnesium stearate.
2. Increase the compression force appropriately during tablet production.
3. Improve granule flow properties through adequate blending and the use of flow agents.
4. Adjust the tablet press settings based on granulation characteristics and compression analysis.
5. Use high-quality and properly stored excipients.
6. Regularly inspect and maintain the tooling to prevent damage or wear.
7. Regular cleaning and maintenance of the tablet press to avoid oil buildup.
8. Control the humidity and temperature of the production area to prevent moisture absorption in the granules.

Chipping:

Two typical categories of tablet physical flaws are shown in fig. The physical flaw shown in Fig. (a), known as chipping, is the loss of a little piece at the cup's borders or surface. In addition to chipping, inadequate inter-granular binding force is thought to be the cause of high friability and low tablet hardness (12). Tablet edges that break when they exit the press or later during handling and coating procedures are referred to as "chipping." Reason: wrong machine settings, particularly a faulty ejection take-off (5).

Fig. 3- Chipping defect in tablet (7)

Causes (5):

1. Sticking on punch faces occurs when the granules stick to the punch faces during compression, resulting in a deterioration of tablet quality.
2. Too-dry granules can lead to a reduction in tablet quality because the granules will not bind together properly during compression.

3. Too much binding can cause chipping at the bottom of the tablet, which affects tablet quality.

Remedies (5):

1. Dry the granules properly or increase lubrication. If the granules are too dry, they may not bind properly during compression, resulting in poor-quality tablets.
2. Moisture plays a crucial role in tablet compression. If the granules are too dry, they may not bind properly. If the granules contain too much moisture, they may stick together, resulting in difficulties in the flow and compression of the granules.

Cracking:

These appear as small, fine cracks on the upper and lower central surfaces of tablets or on the sidewall. Excessive compression and compaction speeds and resulting high-strain elastic and plastic deformations at the micro scale are also known to contribute to crack formation, with a more prevalent appearance of crack formation at higher compression rates (14).

Fig. 4- Cracking defect in tablet (7)

Causes (5):

1. Large granules can lead to poor flow ability, which can cause problems during tablet compression such as uneven tablet weight and poor tablet hardness.
2. Too-dry granules can also lead to poor flow ability and compressibility. This can result in poorly formed tablets or tablets that crumble easily.
3. Tablets expand during storage when they contain moisture or other volatile substances that evaporate over time. This expansion can cause problems with tablet packaging and affect tablet appearance and quality.
4. Granulation that is too cold can result in poor wetting and slow drying, which can lead to uneven granule size and poor flow ability.
5. Granulation that is too warm can cause the active ingredient to degrade, resulting in reduced potency or other quality problems.

Remedies (13):

1. Incorporating additives such as cross-linking agents, reinforcing agents, or plasticizers can also improve the tensile strength of the tablet.
2. Proper drying and curing techniques can enhance the tablet's properties and minimize defects.
3. Coating or laminating the film with other materials can provide additional strength and durability.
4. Molecular orientation techniques can improve the mechanical properties of the tablet.
5. Adding UV stabilizers or other environmental-resistant additives can help protect the tablet from degradation.
6. Adjusting the temperature and pressure during the extrusion process can affect the final properties.

7. Using highly purified raw materials can enhance tablet quality and reduce defects.
8. Conducting in-process testing and quality control can help identify and correct issues during production.
9. Post-process treatments, such as annealing or heat setting, can improve the performance.
10. Improving the overall manufacturing process and equipment can enhance the quality and consistency of the tablet.

Sticking:

In the context of tablet manufacture, "sticking" refers to the adhesion of the active pharmaceutical ingredient (API) or tablet excipients to the surface of the tablet punches during compression. This stickiness can accumulate during batch compression and result in tablet flaws that lower manufacturing productivity and yield. In this article, the term "sticking" is used to represent both "filming," in which a film of particles forms across any area of the punch face, and "picking," in which powder accumulates inside a logo or other embossed area of the punch tip. As batch sizes expand, sticking is frequently first noticed in the later stages of drug product development, during scale-up or commercial-scale manufacturing. By controlling tablet press speeds, compression force, obtaining specialized punch surfaces, or shrinking batch sizes, manufacturing process changes are typically used to reduce or mitigate the sticking problem at this stage in the drug product development cycle because the API and excipient attributes and formulation may be fixed (15).The tablet substance clinging to the die wall is referred to as "sticking." The main cause of filming, a sluggish sort of sticking, is too much moisture in the granulation. Sticking happens when something is inadequately lubricated or dried (16).

Fig. 5- Sticking defect in tablet (7)

Causes (1):

1. The presence of ingredients with low melting points, such as stearic acid and peg (polyethylene glycol), which soften under compressive heat.
2. The grains contain too much moisture.
3. Variations in tablet size and shape can lead to uneven coating, resulting in bare patches on some tablets.
4. Inadequate mixing of the coating solution, resulting in the settling of particles and an unequal distribution of components.
5. Incorrect spray gun technique or poorly maintained equipment can result in uneven spray patterns and poor coating.
6. Insufficient air flow through the coating pan leads to variations in the drying speed of the tablets and an uneven coating.
7. Poor adhesion of the coating solution to the tablet surface is due to low surface tension caused by improper formulation or mixing of the coating solution.
8. Inconsistent pan speed, which can result in insufficient mixing and lead to uneven coating.

Remedies (13):

1. Adjusting the viscosity of the coating solution to help it adhere better to the tablet surface can also be helpful.
2. Improving tablet surface cleanliness by using a dust filter, air showers, or vacuum de-dusting ahead of the coating process can also help.
3. Adding a surfactant to the coating solution can improve the spreading of the coating solution on the tablet surface.
4. Increasing the spraying distance between the nozzle and the tablets to avoid overwetting the tablets
5. Adjusting the atomizing air pressure or changing the spray gun nozzle to achieve a more uniform spray pattern
6. Increasing the pan speed to enhance the tablet movement and improve the coating distribution
7. Using tablets with a more uniform surface to maintain better coating distribution
8. Pre-warming the tablets before coating can increase tablet temperature, which helps reduce surface tension and improve coating adhesion.
9. Ensuring a consistent and appropriate temperature and humidity in the coating environment.
10. Conducting maintenance checks on the coating equipment to ensure it is functioning correctly and efficiently
11. Optimizing the coating process parameters, such as spray rate or spray time, to improve the coating quality and distribution.

Picking

Picking is minimized by properly cleaning and maintaining the punch surfaces. Using a lubricant can also reduce friction and minimize picking. Ensure the granules are fully dry before compressing to prevent compressed granules. Checking and replacing scratched punches can prevent picking caused by damaged surfaces (4).

Fig. 6- Picking defect in tablet (7)

Cause (1):

1. The punch tip engraving, embossing, or debossing The small enclosed areas in the letters like "A," "B," "D," "O," "Q," etc. The punch tips can trap granules during compression, causing them to stick or get trapped, leading to picking.

Remedies (1):

1. Properly drying the granules is essential to preventing moisture-related issues that can contribute to picking. It's important to determine the appropriate optimum moisture limit for the granules prior to compression. This can help reduce the likelihood that granules will stick to the punch faces during compression.
2. Increasing lubrication can also help prevent granules from adhering to punch faces during compression. Colloidal silica can be used as a polishing agent to reduce the surface tension of the granules and

improve lubrication. Additional high-temperature lubricants may also be used to reduce surface friction and stickiness.

3. The use of high-melting-point materials and lubricants can also help prevent picking. These materials can form a protective layer on the surface of the granules, reducing the likelihood that they will stick to the punch tips during compression.
4. Refrigerating the granules and tablet press can also help reduce the incidence of picking. Lowering the temperature can help reduce the adhesion force between the granules and the punch faces, making it less likely for the granules to stick or get trapped.

Binding:

The term "binding in the die" is used when the tablets stick, seize, or rip within the die. The die develops a coating, preventing the tablet from being ejected. The tablet's sides are fractured, and it may break if there is too much binding. Because the tablet material is adhered to the die cavity, it is challenging to remove the tablet from the punches (5).

Fig. 7- Binding defect in tablet (7)

Causes (8):

1. As a result of an inadequate or bad lubricant.
2. Granules that is too damp.
3. Too-big grains.
4. Too-hard granules prevent the lubricant from working properly.
5. Uncomfortably heated granular substance.
6. Because of improperly made dies.
7. Abrasion and corrosion-related rough dies.
8. Because of small deaths.
9. The tablet press applies too much pressure.

Remedies (8):

1. To properly dry the grains.
2. To alter or add lubrication.
3. To decrease the granular size.
4. To alter the granulation process and decrease granular size.
5. To lower the temperature.
6. To properly clean the dies.

Mottling:

Mottling is a common tablet appearance defect that presents as an uneven distribution of color or speckling on the tablet surface. It occurs when there is a variation in the amount or distribution of the colorant used in the tablet formulation. Mottling can affect the aesthetic appearance of the tablet, causing it to look unattractive, and may also suggest a lack of uniformity in the tablet batch. Mottling can be caused by several

factors, including variations in the concentration of colorant, differences in particle size, shape, or density of the tablet excipients, uneven mixing, or inadequate blending of the formulation. Strategies for preventing mottling include optimizing the tablet formulation, using high-quality colorants and excipients, controlling manufacturing process variables such as blending time and mixing speed, and conducting regular quality control checks such as visual inspection and analytical testing.

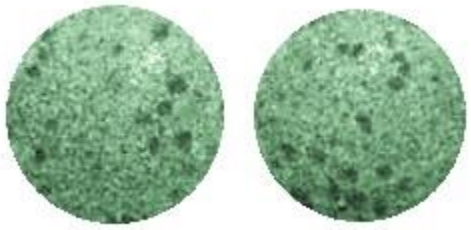

Fig. 8- Mottling defect in tablet (7)

Causes (1):

1. Use of substandard or adulterated ingredients.
2. Differences in manufacturing processes or batch-to-batch variations.
3. Use of different excipients or inactive ingredients in a formulation.
4. Contamination during manufacturing or packaging.
5. Exposure to light, oxygen, moisture, and heat.
6. Interactions between different ingredients in the formulation.
7. Differences in the source or quality of raw materials used in the drug manufacturing process.

Remedies (1):

1. Monitor and control storage conditions such as temperature, humidity, and lighting.
2. Source ingredients from reputable and reliable suppliers.
3. Maintain consistent manufacturing processes and quality control measures.
4. Test for impurities and degradation products during quality control testing.
5. Use appropriate packaging materials to prevent contamination and protect against degradation.
6. Conduct stability studies to determine shelf life and optimal storage conditions.
7. Implement good manufacturing practices (GMP) to ensure high quality standards are maintained throughout the manufacturing process.
8. Regularly inspect and audit manufacturing facilities to ensure compliance with regulatory standards and guidelines.

Double impression:

Owing to the unrestricted rotation of punches with engraved or monogrammed faces. The punch spins as he moves freely, and at this moment, the punch can leave a second imprint on the tablet's bottom, creating a double impression (8).

Fig. 9- Double impression defect in tablet (7)

Causes (5):

1. Unequal pressure is applied on the upper punch and lower punch during ejection due to improper die design or improper adjustment of the tablet press machine.
2. Insufficient lubrication of the punch faces or punch guide.
3. Damage or wear and tear on the punch faces or punch guide.
4. Misalignment of the punch guide or tablet press machine components.
5. Inconsistent or improper filling of the powder in the die cavity.
6. Over-compression of the powder during tablet compression, causing the tablet to stick to the punch faces.
7. Inconsistent tablet weight or thickness due to variations in the powder or compression process.
8. Improper or insufficient cleaning of the tablet press machine.
9. Operator error or lack of training in proper tablet press machine operation.

Remedies (5):

1. Adjust the lower punch and upper punch to ensure equal pressure and force during ejection.
2. Regularly lubricate the punch faces and punch guide to minimise friction and wear and tear.
3. Inspect punches, punch guides, and dies regularly to ensure they are in good condition and replace any damaged parts.
4. Properly align all components of the tablet press machine to prevent misalignment issues.
5. Use consistent and proper filling techniques to ensure uniform powder distribution and prevent over-compression of the powder during tablet compression.
6. Monitor and adjust the compression force to prevent over-compression of the powder.
7. Implement regular cleaning and maintenance of the tablet press machine to prevent issues related to cleanliness and wear and tear of components.
8. Provide proper training for operators to prevent operator errors and ensure proper operation of the tablet press machine.

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