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Tablet Formulation and Defects of Tablets – A Review

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ABSTRACT
Sources behind Defected tablet formulation is due to improper compression of granules in compression machine, size of punching cavity is also a source in defected tablet formulation. For tablet formulation we use Excipients like Diluents, Binders, Lubricants, Colour, etc. Excipients are the materials used other than active pharmaceutical active ingredients to produce standard quality tablets. Poor quality and purity of excipients can produce defects in tablets. Quality of raw material of Active ingredient is also a source of defect in tablets. Improper mixing of active ingredient and excipients is also a source of defects in tablet. Drying at high temperatures that may occurs blistering in tablets. Standard tablets formulation is totally depending on Chemical and Physical properties of excipients and active ingredients. Cracking, Chipping, Blooming, Colour variation are most common defects in tablets. Improper coating of tablets may produce defects in tablets. Technique formulation of tablet is also a source of defect. Techniques like wet granulation, dry granulation which are initial process of tablet formulation. Flow properties of material also play an important role in standard tablet formulation. Properties of material like density, particle size, particle shape, surface area, angle of repose, Housner's ratio. These all are main sources of defects in tablet formulation. This article on these variations.it pinpoint the possible causes of these defects and offers advice on preventing and fixing the source of the problems.

KEY WORDS: - Cracking, Chipping, Blooming, Colour variation, formulation, granulation, Rf value.

I. INTRODUCTION

Tablets are the solid Pharmaceutical dosage form which contains drug/sand excipients. Tablets are manufactured by 2 methods, Compression method and molding method, and administered through Oral ,Sublingual, Buccal and Vaginal route. To manufacture an ideal tablets, it is necessary to perform Pre-formulation studies. Now pre-formulation studies are study of Physicochemical characteristics of drug substances. Physicochemical characteristics are the study of chemical and physical properties of a drug substance. Characterization of drug molecule is major step in product development. Pre-formulation studies are conducted to collect all necessary data on drug substances, excipients and packaging materials that may affects formulation, method of manufacturing, pharmacokinetics and bioavailability of drug.

PHISICAL PROPERTIES:-

Organoleptic Properties:- Evaluation of drug on the basis of color, texture and taste. Because it should be in good appearance, color should be appealing to eye, taste and odour.

Purity studies are essential for further studies to be carried out safely because impurities may make a compound toxic or render it unstable. Thin layer chromatography (TLC),High pressure liquid chromatography(HPLC), Gas chromatography(GC). These techniques are used to determine impurity index(II) and Homogeneity index(IH).

Particle size, Shape and Surface area are the properties of drugs that affect biopharmaceutical behavior. The big difference in the particle size affect flow properties of powder and cause impair mixing efficiency. Fine powder is also susceptible to attack by heat or atmosphere or light or humidity which further cause stability issues. The methods used to obtain particle size distribution are Microscopy, Optical microscopy, Sieving, Sedimentation rate, Elutriation studies, Centrifugal studies, Permeability studies, Light scattering. Shape and surface properties affects flow and dissolution. Shape Factor is determined which is the ratio of the longest to the shortest dimensions. Surface area may be determined by the BET equation based on the theory of absorption.

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DENSITY

A property that provides the characterization of the flow ability of the powders.

1. True Density

Density of sample excludes the volume of the pore and voids within the sample .

True density= Weight of powder .
True volume of powder

2. Bulk Density

Mass of powder divided by the bulk volume

Bulk density= M
V

FLOW PROPERTIES

Powder flow properties are characterized by determining angle of repose, Compressibility index, Hausner ratio.

Compressibility index =
(tapped density-Bulk density) 100
Tapped density

Hausner ratio = tapped density
Bulk density

Angle of repose =tan-1 height of pile
Radius of pile

Solubility Profile

Defined as the amount of the drug (solute) that dissolves in a given solution (solvent) to obtain a saturated solution, Solubility is an essential and important pre formulation parameter before designing of dosage form.

IONIZATION CONSTANT (pKa)

Drugs are either weak acids or weak bases. Absorption is dependant to a large extent on their degree of ionization. Un-ionized drugs are lipid-soluble and transported by passive diffusion across the membrane.

pKa for acidic drugs:
pH = pKa+log (ionized drug) / (unionized drug)
For basic drugs:
pH = pka + log (unionized drug) / (ionized drug)

PARTITION COEFFICIANT

Partition coefficient are useful to formulator in selecting appropriate extraction solvents.

DISSOLUTION

Dissolution is the process by which a solid substance enters the solvent phase to yield a solution so that body can absorb drug easily. Dissolution rate can affect the onset and intensity of the drug.

STABILITY ANALYSIS

Stability analysis is done to generate useful information on how environmental factor like, temperature, humidity, light etc. influence the quality of the drug products over time.

Solid state stability analysis:- Important aspect of drug stability testing. Identifies stable storage condition for drugs. Also helps in identification of compatible excipients for a formulation. The data generated by this analysis is influenced by temperature ,pH, humidity, hydrolysis, oxidation.

Solution state stability analysis:-This analysis helpful for pre-formulation processes. Degradation in solution s much faster than dry form. It effects of pH on stability is important in the development of both oral and parenteral dosage form.

Drug-excipient compatibity studies:- Compatibility study is very important and useful to the formulator for the selection of appropriate excipients for dug product. In pharmaceutical formulation, drug substance with one or more excipients may undergo chemical and physical interaction.

CHEMICAL PROPERTIES

HYDROLYSIS:- Breaking of molecule is due to reaction with water called as hydrolysis. It is an step of degradation of drug or substance. Drug like ester, amides lactams undergo hydrolysis. Reaction between ionic drugs proceed faster than with neutral molecules.

OXIDATION AND REDUCTION

Oxidation and reduction are the common pathway for drug degradation in liquid and solid formulation. Oxidation means loss of electron while reduction means gain of electron.

RECEMIZATION

Interconversion of one isomer into other alter pharmacokinetic, pharmacological and toxicological properties. For example levo-Cetirizine more active than Cetirizine.

In formulation of ideal dosage form it is very important to study pre-formulatiuon parameter. Prefomulatory studies helps in formulation of Ideal and stable product.

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II. MATERIAL AND METHODS

In this article we will discus about sources of defects in tablet formulation and it's precautions.

The defects due to Processing Method

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

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

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

The defects due to Excipient

Chipping: It is due to very dry granules.

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

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

Binding: These problems like chipping, sticking, picking are due to more amount of binder in the granules or wet granules.

The defect due to other factors

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 due to Machine

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.

The Sources and Precautions of Capping Related To Formulation (Granulation)

Sources

Large amount of fines in the granulation

Too dry or very low moisture content (leading to loss of proper binding action).

Not thoroughly dried granules.

Insufficient or improper lubricant.

Precautions

Remove some or all fines through 100 to 200 mesh screen.

Moisten the granules suitably. Add hygroscopic substance e.g.: sorbitol, methyl cellulose or PEG-4000.

Dry the granules properly.

Increasing the amount of binder.

Compress at room temperature.

The Sources AND Precautions Of Capping Related To Machine

SOURCES

Poorly finished dies

Deep concave punches or bevelled-edge faces of punches.

Lower punch remains below the face of die during ejection.

Precautions

Polish dies properly. Investigate other steels or other materials.

Use flat punches.

Make proper setting of lower punch during ejection.

Adjust sweep-off blade correctly to facilitate proper ejection.

LAMINATION

Lamination is the separation of a tablet into two or more distinct horizontal layers. Reasons Air–entrapment during compression and subsequent release on ejection.

The condition is exaggerated by higher speed of turret.

The Causes and Remedies of Lamination Related ToFormulation (Granulation)

SOURCES

Oily or waxy materials in granules.

Too much of hydrophobic lubricant.

PRECAUTIONS

Modify mixing process

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Use a less amount of lubricant or change the type of lubricant.

The SOURCES AND PRECAUTIONS Of Lamination Related To Machine(Dies,Punches And Tablet Press)

SOURCES
Rapid relaxation of the peripheral regions of a tablet, on ejection from a die.
Rapid decompression
Remedies
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.

SOURCES
Incorrect machine settings, specially mis-set ejection take-off.

The SOURCES AND PRECAUTION Of Chipping Related ToFormulation (Granulation)

SOURCES
Sticking on punch faces
Too dry granules.
Too much binding causes chipping at bottom.

PRECAUTIONS
Dry the granules properly or increase lubrication.
Moisten the granules to plasticize. Add hygroscopic substances.

The SOURCES ANDPRECAUTIONS Of Chipping Related To Machine' (Dies, Punches And Tablet Press)

SOURCES
Barreled die (centre of the die wider than ends)
Edge of punch face turned inside/inward.
Concavity too deep to compress properly.

PRECAUTION
Polish the die to make it cylindrical
Polish the punch edges
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.

The SOURCES AND PRECAUTION Of Cracking Related To Formulation (Granulation)

SOURCES
Large size of granules.
Too dry granules.
Tablets expand.

PRECAUTIONS
Reduce granule size. Add fines.
Moisten the granules properly and add proper amount of binder.
Compress at room temperature.

The SOURCES AND PRECAUTION Of Cracking Related To Machine (Die Punches And Tablet Press)

SOURCES
Tablet expands on ejection due to air entrapmentDeep concavities cause cracking while removing tablets

PRECAUTIONS
Use tapered die.
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.

The SOURCES AND PRECAUTIONS Of Sticking Related To Formulation (Granulation)

SOURCES
Granules not dried properly.
Too little or improper lubrication.
Too much binder. Too soft or weak granules.
PRECAUTIONS
Dry the granules properly. Make moisture analysis to determine limits.
Increase or change lubricant.

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Reduce the amount of binder or use a different type of binder.

The SOURCES AND PRECAUTIONS Of Sticking Related To Machine (Dies, Punches And Tablet Press)

SOURCES
Concavity too deep for granulation.
Too little pressure.
Compressing too fast.

PRECAUTIONS
Reduce concavity to optimum.
Increase pressure.
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.

The SOURCES AND PRECAUTIONS Of Picking Related To Formulation (Granulation)

SOURCES
Excessive moisture in granules.
Too little or improper lubrication.
Low melting point substances, may soften from the heat of compression and lead to picking.
Too warm granules when compressing. Too much amount of binder.

PRECAUTIONS
Add high melting-point materials. Use high meting point lubricants.
Refrigerate granules and the entire tablet press.
Compress at room temperature. Cool sufficiently before compression.
Reduce the amount of binder, change the type or use dry binders.

The SOURCES ANDPRECAUTIONS Of Picking Related ToMachine (Dies, Punches And Tablet Press)

SOURCES
Bevels or dividing lines too deep.
Pressure applied is not enough; too soft tablets.

PRECAUTIONS
Polish faces to high luster.
Design lettering as large as possible.
Plate the punch faces with chromium to produce a smooth and non-adherent
face.
Reduce depths and sharpness.
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.

The SOURCES AND PRECAUTIONS Of Binding Related To Formulation (Granulation)
SOURCES
Too moist granules and extrudes around lower punch.
Insufficient or improper lubricant.
Too coarse granules.
Too hard granules for the lubricant to be effective.

PRECAUTIONS
Modify granulation. Reduce granular size.
If coarse granules, reduce its size.
Use wear-resistant dies.
Reduce temperature.
Increase clearance if it is extruding.

The SOURCES AND PRECAUTIONS Of Binding Related To Machine (Dies, Punches And Tablet Press)

SOURCES
Poorly finished dies.
Rough dies due to abrasion, corrosion.
Undersized dies. Too little clearance.
Too much pressure in the tablet press.

PRECAUTIONS
Polish the dies properly.

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Investigate other steels or other materials or modify
granulation.
Rework to proper size. Increase clearance.
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.

The SOURCES AND PRECAUTIONS Of Mottling

SOURCES
Coloured drug used with colourless excipients
Improper mixing

PRECAUTIONS
Use appropriate colourants.

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.

The SOURCES AND PRECAUTIONS Of Blistering

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

PRECAUTIIONS
Use mild drying condition.

CRATERING
It is defect of film coating whereby volcanic-like craters
appears 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.

The SOURCES AND PRECAUTIONS Of Cratering

SOURCES
Inefficient drying.
Higher rate of application of coating solution.

PRECAUTIONS
Use efficient and optimum drying conditions.
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 SOURCES AND PRECAUTIONS Of Picking

SOURCES
Inefficient drying.
Higher rate of application of coating solution.

PRECAUTIONS
Use optimum and efficient drying conditions or increase the inlet air temperature.
Decrease the rater 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.

The SOURCES AND PRECAUTIONS Of Pitting

SOURCES
Inappropriate drying (inlet air) temperature.

PRECAUTIONS
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.

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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.

The SOURCES AND PRECAUTIONS Of Blooming

SOURCES

High concentration and low molecular weight of plasticizer.

PRECAUTIONS

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.

The SOURCES AND PRECAUTIONS Of Blushing

Causes

High coating temperature.

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.

PRECAUTIUONS

Decrease the drying air temperature.

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.

The SOURCES AND PRECAUTIONS Of Colour Variation

SOURCES

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

PRECAUTIONS

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.

The SOURCES AND PRECAUTIONS Of Infilling

SOURCES

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

PRECAUTIONS

Add alcohol or use spray nozzle capable of finer atomization.

CONCLUSION AND RESULT

Studies From this article provides the sources and precautions related to defects in formulation of the ideal tablet. Defects in tablets can arise during manufacturing processes, storage and transport. Tablets are most common used among oral dosage form, because it is easy to administer and low cost. This article focus to establish ways to resolve defects at the tablet press and identify the main reason of sources and we resolved the defects of tablets with the help of this review article

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