Review on Tablet Formulation

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***Abstract*: Medicines are not only a science; it is also an art. It does not consist of compounding pills and plasters; it deals with the very processes of life, which must be understood before they may be guided. Pharmaceutical oral solid dosage forms have been used widely for decades mainly due to their convenience of administration and their suitability for delivery for delivery of drugs for systemic effects. The tablets can be made directly from powders or from granules pellets, or from film-coated multiple units. Tablets are now the most popular dosage form, accounting for some 70% of all ethical pharmaceutical preparations produced. Tablets may be defined as solid pharmaceutical dosage forms containing drug substances with or without suitable diluents and prepared by either compression or moulding methods. Hence, tablets can be broadly classified as compressed tablets and moulded tablets. Compressed tablets can be further classified as directly compressible tablets, chewable tablets and tablet triturates etc.**

***Keywords*: film-coated, chewable tablets, Sweetening agents, multi-layer tablet, Dry granulation.**

Introduction

According to USP, Tablet is defined as a compressed solid dosage form containing medicaments with or without Excipients. According to the Indian Pharmacopoeia, Pharmaceutical tablets are solid, flat or biconvex dishes, unit dosage form, prepared by compressing a drug or a mixture of drugs, with or without diluents.

They are easy to carry, easy to swallow and they are attractive in appearance. Unpleasant taste can be masked by sugar coating and they do not require anymeasurement of dose. Some of the tablets are divided into halves and quarters by drawing lines during manufacturing to facilitate breakage whenever a fractional doseis required. Solid medicaments may be administered orally as powders, pills, cachets,capsules or tablets. These dosage forms contain a quantity of drug which is given as a single Unit and they are known collectively as solid unit dosage forms, even in thecase of Sustained action preparations which, technically, contain the equivalent of several Normal doses of drug .The stringent formulation requirements of modern Medicaments, the many advantages of tablet and capsule medication, coupled With expanding health services and the commitment need for large- scale Economic manufacture, have led to a steady decline in the prescribing of powders Andpills .Tablets and capsules, on the other hand, currently account for well over Twothird of the total number and cost of medicines produced all over the world. Tabletsare solid dosage form which is the conventional as well as have many advantagesover other dosage forms. Tablets are the most popular dosage form about 70% ofthe total medicines are dispensed in the form of tablet. Tablets had different shapes,sizes, as well as weight depending on medicinal substances and the intended modeof administration. In this paper some advantages as well as some disadvantages of tablets, the basic.

Advantages & Disadvantages

Advantages of tablet dosage form over other oral drug delivery systemsfrom patients stand point

They are easy to carry, easy to swallow and they are attractive in appearance. Unpleasant taste can be masked by sugar coating and they do not require anymeasurement of dose.

Some of the tablets are divided into halves and quarters by drawing lines duringmanufacturing to facilitate breakage whenever a fractional dose is required.

From the standpoint of manufacturer:

- Tablets provide best combined properties of chemical, mechanical andmicrobiological stability of all the oral dosage forms.
- Since they are generally produced on a large scale, therefore, their cost of production is relatively low, hence economical. They are in general the easiestand cheapest to package and ship among all oral dosage forms.
- Some specialized tablets may be prepared for modified release profile of the drug.
- Product identification is potentially the simplest and cheapest requiring no additional processing steps when employing an embossed or monogrammedpunch face.

Disadvantages of tablet dosage form

- Difficult to swallow in case of children and unconscious patients.

- Drugs with poor wetting, slow dissolution properties, optimum absorption high in GIT may be difficult to formulate or manufacture as a tablet that will still provide adequate or full drug bioavailability.

Types of tablets

(a) Tablets ingested orally:

- Compressed tablets
- Multiple compressed tablets
- Enteric coated tablets
- Sugar coated tablets
- Film coated tablets
- Chewable tablets

(b) Tablets used in the oral cavities:

- Buccal Tablets
- Sublingual tablets
- Lozenges
- Dental cones

(c) Tablets administered by other routes:

- Implantation tablets
- Vaginal tablets

(d) Tablets used to prepare solutions:

- Effervescent tablets
- Dispensing tablets
- Hypodermic tablets
- Tablet triturates

(a) Tablets ingested orally-

(1) Compressed tablets: -

- These tablets are formed by compression and contain no special coating. They are made from powdered, crystalline or granular materials, alone or in combination with suitable excipients.
- These tablets contain water soluble drugs which after swallowing get disintegrated in the stomach and its drug contents are absorbed in the gastrointestinal tract and distributed in the whole body. e.g., Aspirin (Disprin) paracetamol tablets (Crocin).

(2) Multiple compressed tablets / Layered tablets-

- These are compressed tablets made by more than one compression cycle. Such tablets are prepared by compressing additional tablet granulation on a previously compressed granulation. The operation may be repeated to produce multilayered tablets of two or three layers.
- To avoid incompatibility, the ingredients of the formulation except the incompatible material are compressed into a tablet and then incompatible substance along with necessary excipients are compressed over the previously compressed tablet.

(3) Sustained action tablets:

These are the tablets which after oral administration release the drug at a desired timeand prolong the effect of the medicament. These tablets when taken orally release themedicament in a sufficient quantity as and when required to maintain the maximum effective concentration of the drug in the blood throughout the period of treatment.
e.g. Diclofenac SR tablets.

Enteric coated tablets:

- These are compressed tablet meant for administration by swallowing and are designed to by-pass the stomach and get disintegrated in the intestine only.
- These tablets are coated with materials resistant to acidic pH (like cellulose acetate phthalate, CAP) of the gastric fluid but get disintegrated in the alkaline pH of the intestine.

(4) Sugar coated tablets:

- These are compressed tablets containing a sugar coating. Such coatings are done to mask the bitter and unpleasant odour and the taste of the medicament. The sugar coating makes the tablet elegant and it also safeguard the drug from atmospheric effects.

(5) Film coated tablets:

- The compressed tablets having a film coating of some polymer substance, suchas hydroxy propyl cellulose, hydroxy propyl methyl cellulose and ethyl cellulose.
- The film coating protects the medicament from atmospheric effects. Film coated tablets are generally tasteless, having little increase in the tablet weight and have less elegance than that of sugar-coated tablets.

(6) Chewable tablets:

- These are the tablets which are required to be broken and chewed in between the teeth before ingestion. These tablets are given to the children who have difficulty in swallowing and to the adults who dislike swallowing.
- These tablets should have very acceptable taste and flavor. Ex- Antacid tablets (Diginet).

(b) Tablets used in oral cavity

(1) Buccal tablets:

- These tablets are to be placed in the side of the cheek (buccal pouch) where they dissolve or erode slowly and are absorbed directly in the buccal cavity without passing into the alimentary canal.
- Therefore, they are formulated and compressed with sufficient pressure to givea hard tablet. e.g., Progesterone tablets.

(2) Sublingual tablets:

- These tablets are to be placed under the tongue where they dissolve or disintegrate quickly and are absorbed directly without passing into GIT. e.g. tablets of nitroglycerin, isoproterenol hydrochloride or erythrityl tetranitrate.

(3) Lozenges tablets:

- These tablets are designed to exert a local effect in the mouth or throat. These tablets are commonly used to treat sore throat to control coughing in common cold. They may contain local anaesthetics, antiseptics, antibacterial agents and astringents.
- These are prepared by compression at a high pressure by the moulding process and generally contain a sweetening agent, flavoring agent and a substance which roducesa cooling effect. e.g., Vicks lozenges, Strepsils.

(4) Dental cones:

- These are compressed tablets meant for placement in the empty sockets after tooth extraction. They prevent the multiplication of bacteria in the socket following such extraction by using slow-releasing antibacterial compounds or to reduce bleeding by containing the astringent.
- These tablets contain an excipient like lactose, sodium bicarbonate and sodium chloride. These cones generally get dissolved in 20 to 40 minutes time.

(c) Tablets administered by other routes(1) Implantation Tablets:

- These tablets are placed under the skin or inserted subcutaneously by means of minor surgical operation and are slowly absorbed. These may be made by heavy compression but are normally made by fusion. The ***implants must be sterile*** and should be ***packed individually in sterile*** condition. Implants are mainly used for the administration of hormones such as testosterone steroids for contraception. These tablets are very usefully exploited for birth control purpose in human beings.
- The disadvantages of implant tablets are their administration, changing rate of release with change of surface area and possibility of tissue reactions.

(2) Vaginal tablets:

- These tablets are meant to dissolve slowly in the vaginal cavity. The tablets aretypically ovoid or pear shaped for the ease of insertion. these tablets are used to release steroids or antimicrobial agents. the tablets are often buffered to promote a pH favorable to the action of a specified antimicrobial agent. The contains easily soluble components like lactose or sodium bicarbonate.

(d) Tablets used to prepare solutions(1) Effervescent tablets:

- These tablets along with the active medicament contain ingredients like sodium bicarbonate, citric acid and tartaric acid which react in the presence of water liberating carbon dioxide and producing effervescence leading to disintegration of the tablet, thus fastens solution formation and increase the palatability. E.g., Histac (Ranitidine)

(2) Dispensing tablets:

- These tablets provide a convenient quantity of potent drug that can be readily convert into powders and incorporate into liquids, thus circumventing thenecessity to weigh small quantities. these tablets are supplied primarily as a convenience for extemporaneous compounding and should never be dispensed as dosage form.

- e.g., The drugs commonly incorporated are mild silver potentiate, bichloride of mercury merbromin an quaternary ammonium compound.

(3) Hypodermic tablets:

- Hypodermic tablets are soft, readily soluble tablets and originally were usedfor the preparation of solutions to be injected. These tablets are dissolved in sterile water or water for injection and administered by parenteral route. these tablets are not preferred now-a-days because the resulting solution is not always sterile.

(4) Tablet triturates (Moulded tablets):

- These are powders moulded into tablets. They are flat, circular discs, usually containing potent substance mixed with lactose, lactose and sucrose, dextrose,or another suitable diluent.
- Since they are intended to disintegrate very quickly in contact with moisture, water insoluble adjuncts are avoided. The name ‘tablet triturate’ is appropriate because they usually contain triturations (*trituration = dilution with an inert substance*).

Tablet Ingredients/ Excipients-

In addition to active ingredients, tablet contains a number of inert materials known asadditives or excipients. Different excipients are:

1. Diluent / Filler
2. Binder and adhesive
3. Disintegrants
4. Lubricants and glidants
5. Coloring agents
6. Flavoring agents
7. Sweetening agents

Function of excipients-

- Impart weight, accuracy, & volume.
- Improve solubility
- Increase stability
- Enhance bioavailability
- Modifying drug release
- Assist product identification
- Increase patient acceptability
- Facilitate dosage form design

1. Diluents

Definition- Diluents are fillers used to make required bulk of the tablet when the drugdosage itself is inadequate to produce the bulk.

Secondary reason is to provide better tablet properties such as improve cohesion, topermit use of direct compression manufacturing or to promote flow.

properties:

1. They must be non-toxic and low cost.
2. They must be commercially available in acceptable grade
3. They must be physiologically inert, physically & chemically stable by themselves & in combination with the drugs.
4. They must be free from all microbial contamination.
5. They do not alter the bioavailability of drug.
6. They must be color compatible.

Lactose

- Lactose is the most widely used diluent for tablet formulation. It is obtained in hydrous and anhydrous form. The anhydrous form, picks up moisture when exposed to elevated humidity. Such tablets should be packed in moisture proof packets or containers. When a wet granulation method is employed, the hydrousform of lactose should generally be used.
- Two grades of lactoses are commercially available:

(i) A 60 to 80 mesh – coarse

(ii) a 80 to 100 mesh – regular grade

Starch

Starch may be obtained from corn, wheat or potatoes and rice. It is occasionally used as a tablet diluent. USP grade of starch is usually possesses moisture content between 11 to 14%. Specially dried types of starch that have a standard moisture level of 2-4% are available, but are costly. Use of such starches in wet granulation is wasteful since their moisture level increase to 6-8% following moisture exposure.

Directly compressible starches

Sta–Rx 1500– free flowing, directly compressible starch. It is used as diluent, binder,disintegrant.

Emdex and Celutab – are two hydrolyzed starches – contains dextrose90–92%andmaltose 3–5free flowing and directly compressible and may be usedin place or mannitol in chewable tablets because of their sweetness and smooth feeling in the mouth.

Dextrose (D–Glucose)

Available in two forms: as hydrates and anhydrous forms. Dextrose may sometimes becombined in formulation to replace some of the spray-dried lactose, which may reduce the tendency of the resulting tablets to darken.

Sorbitol

It is an optical isomer of mannitol and is sometimes combined with mannitol formulations to reduce the diluent cost.

Disadvantages: - It is hygroscopic at humidifiesabove 65%.

Sucrose

Some sucrose-based diluents are:

Sugar tab– 90 to 93% sucrose + 7 to 10% invert sugarDi Pac – 97% sucrose + 3% modified dextrin's Nu Tab– 95% sucrose + 4% invert sugar + small amount of corn starch + Mg stearateAdvantages: They are all used for direct compression.
Disadvantages: All are hygroscopic when exposed to elevated humidity.

2. Binders and Adhesive

Definition- Agents used to impart cohesive qualities to the powdered material arereferred toas binders or granulators.

Objective of incorporating binders

They impart a cohesiveness to the tablet formulation (both direct compression and wet–granulation method) which ensures the tablet remaining intact after compression.

They improve the free-flowing qualities by the formation of granules of desired sizeand hardness.

S**tarch paste**

Corn starch is often used in the concentration of 10–20%.

Method of preparation: - Corn starch is dispersed in cold purified water to make a 5 to10% w/w suspension and then warming in water both with continuous stirring until a translucent paste is formed. (Actually, hydrolysis of starch takes place.)

Liquid glucose: - 50% solution in water is fairly common binding agent.

Sucrose solution: - 50% to 74% sugar solution is used as binder. They produce hard but brittle granules. Their cost is low.

Gelatin solution

Concentration 10–20% aqueous solution

Should be prepared freshly and added in warm condition otherwise it will becomesolid.

Method of preparation

The gelatin is dispersed in cold water and allowed to stand until hydrated. The hydratedmass is warmed in water bath to dissolve.

Cellulosic solutions

HPMC (Hydroxy propyl methyl cellulose) Soluble in cold water.

Method of preparation: HPMC is dispersed in hot water, under agitation. The mixture iscooled as quickly as possible and as low as possible

HEC (Hydroxy ethyl cellulose), HPC (Hydroxy propyl cellulose) are other successfulbinders.

PVP (Polyvinylpyrrolidone) Used as an aqueous or alcoholic solution. Concentration2% and may vary.

Disintegrants

Definition: - A disintegrant is a substance to a mixture of substances, added to tablet to facilitate its breakup or disintegration after administration in the GIT. The active ingredients must be released from the tablet matrix as efficiently as possible to allow for its rapid dissolution. Disintegrants can be classified chemically as: Starches, clays, celluloses, alginates, gums and cross-linked polymers.

Starch

Corn starch, potato starch.

For their disintegrating effect starches are added to the powder blends in dry state.

Mode of action:

Starch has a great affinity for water and swells when moistened, thus facilitatingthe rupture of the tablet matrix.

Others have suggested that the spherical shape of the starch grains increases the porosityof the tablet, thus promoting capillary action.

Normally 5% w/w is suggested and for rapid disintegration 10 – 15% w/w may betaken.

Super disintegrants

Super disintegrants like Croscarmellose - cross linked cellulose, Crospovidone - cross linked polyvinyl pyrrolidone and Sodium starch glycolate- cross linked starch

Mode of action

Croscarmellose swells 4 to 8-fold in less than 10 seconds Crospovidone acts by wickingor capillary action. Sodium starch glycolate swells 7 to 12 folds in less than 30 seconds.

Other materials

Methylcellulose, Agar, Bentonite, Cellulose, Alginic acid, Guargum, and Carboxymethyl cellulose.

Sodium lauryl sulfate is a surfactant. It increases the rate of wetting of the tablet, thus decreases the disintegrating time.

Coloring agent

Dyes are dissolved in the binding solution prior to the granulating process. However, during drying their color may migrate to the surface and may produce mottling of the tablet. So, another approach is to adsorb the dye on starch or calcium sulfate from its aqueous solution; the resultant powder is dried and blended with other ingredients. Color lakes are dyes which are adsorbed onto a hydrous oxide of a heavy metal (like aluminum) resulting in an insoluble form of the dye.

Flavours and Sweeteners

Flavours are usually limited to chewable tablets or other tablets intended to dissolvein the mouth. Flavor oils are added to tablet granulations in solvents, are dispersed onclays and other adsorbents or are emulsified in aqueous granulating agents (i.e., binder).

Manufacturing of Tablets

Manufacture of tablets involves certain well-defined *steps*: namely: -

- ❖ Pulverization and mixing.
- ❖ Granulation.
- ❖ Compression.
- ❖ Coating (if required)

Pulverization and mixing-

In this step the different solid / powder ingredients are reduced to the same particle sizesince particles of different sizes will segregate while mixing.

Various equipment's like Cutter mill, Hammer mill, Roller mill and Fluid energy mill isrequired to reduce the large lumps.

Granulation Technology-

Granulation: It is the process in which primary powder particles are made to adhere to form large multi-particle entities. Range of size: 0.2 mm to 4 mm. (0.2 mm to 0.5 mm)

Wet Granulation-

Step-I Milling of the drug and excipients

Milling of the active ingredients, excipients etc. are milled to obtain a homogeneity inthe final granulation.

If the drug is given in solution, then during drying it will come up to the surface. Toavoid this problem drug is mixed with other excipients in fine state.

Step-II Weighing

Weighing should be done in clean area with provision of air flow system.

In the weighing area all the ingredients must not be brought at a time to avoid cross- contamination.

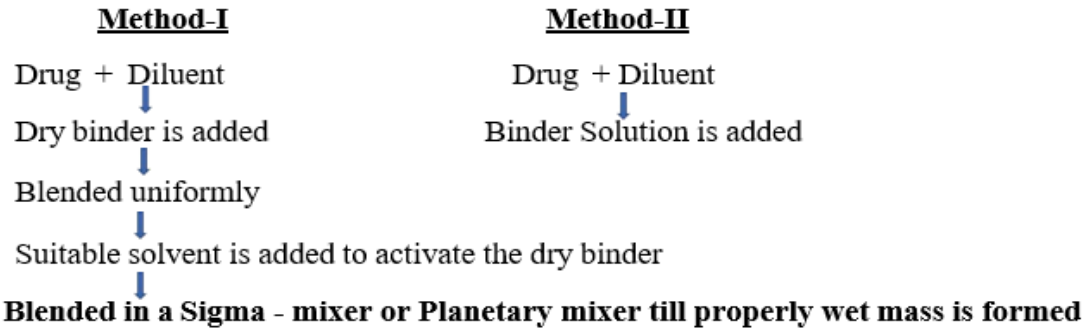
Step-III Mixing Commonly used blenders are:

(a) Double cone blender
(b) V – blender
(c) Ribbon blender
(d) Planetary mixer

Any one of the blenders may be used to mix dry powder mass.

Step-IV Wet Massing

Wet granulation forms the granules by binding the powders together with anadhesive. Binder solutions can be added in two methods:



(i) a small quantity of solvent is permissible, **method-I** is adopted and

(ii) a large quantity of solvent is required **method-II** is adopted.

However, **method-II will give more cohesiveness** than **method-I** if the amountof binder remains constant.

If **granulation is over-wetted**, the granules will be hard, requiring considerable pressure to form the tablets, and the resultant tablets may have a mottled appearance.

If the powder mixture is not wetted sufficiently, the resulting granules will be too soft,breaking down during lubrication and causing difficulty during compression.

Step-V Drying

Drying is usually carried out at **60^0C.** Depending on the thermolabile nature of thedrug the temperature can be optimized. Drying is required in all wet granulation procedures to remove the solvent, but is not dried absolutely because it will pose problems later on. Hence, certain amount of moisture (1 – 4 %) is left within the granules – known as the *residual moisture*.

Methods: Drying can be carried out

Tray dryers – it may take 24 hrs. of drying

Truck dryers – the whole cabinet can be taken out of the dryer

Fluid-bed dryer – carry out drying in 30 mins.

Step-VI Dry Screening

After drying, the granules are make monosize by passing through **mesh screen**.

For drying granules, the screen size to be selected depends on the diameters of thepunch. The following sizes are suggested:

Dry Granulation

Dry granulation is followed in situations **where** (i) the effective dose of a drug is too high for direct compaction and (ii) if the drug is sensitive to heat, moisture or both, which precludes wet granulation. e.g., many aspirin and vitamin formulations are prepared for tableting by compression granulation.

Steps of granulations

Steps of granulations

Milling→ Weighing → Screening → Blending → Slugging → Granulation (Dry) →
Lubrication Compaction.

Slug:

Slug may describe as poorly formed tablets or, may be described as compacted mass of powdered material. *Purpose*: To impart cohesiveness to the ingredients, so asto form tablets of desired properties.

Method: It is done either by

(i) high-capacity heavy duty tablet press

(ii) Chilson Tor roller compactor.

Direct Compression Method-

Milling ⟶ Weighing ⟶ Sieving ⟶ Blending ⟶ Compression

Advantages:

(i) It is much quicker than any of the previous process

(ii) Minimum number of steps are required.

Modified diluents, binders etc. are available in the market which assure spherical shapeof the granules to modify flow property. However, they are not used extensively. If active medicament is less in amount then there will be no problem but in case of high dose large amount of active ingredient is to be replaced by specially treated vehicles toimprove flow property or compressibility. These specially treated materials are **costly**.

- **Tablet Compression**

It can **r**educe the volume by apply pressure, particle in die are re-arrange, resulting a closer packing structure and reduce space and at certain lode reduced space and increase inter- particulate friction will prevent farther interparticle friction.

Elastic deformation: - Either whole or a part can change their shape temporarily.

Plastic deformation: - Change shape permanently.

Particle fragmentation: - Fracture into a number of smaller discrete particles. Find new position- decrease the volume of powder bed- when force increase new particleagain under go deformation-particle particle bonds can formed.

Time of loading: - Deformation of particle are **time independent** process in Elastic& Plastic deformation.

Deformation is time dependent, when its behavior is referred to Viscoelastic &Viscous deformation.

Degree of deformation:- Some quantitive change in shape.

Mode of deformation: - type of shape change. **Basic Component of Compression Machine Head**- Contain upper punch's, dies, lower punches. **Body**- Contain operating machineries.
Hopper- Holding feeding granules.

Dies- Define size, shape of tablet.

Punches – For compression with in dies.

Cam tracks – Guiding the movement of punches.

Feed frame- Guiding the granules from hopper to dies.

Upper turret- Holds the upper punches. **Lower turret**- Hold the lower punch's. **Dietable**- Contain the dies.
Single station – stamping press Multi-station- Rotary press

Fig. 1. Tablet Compression Machine.

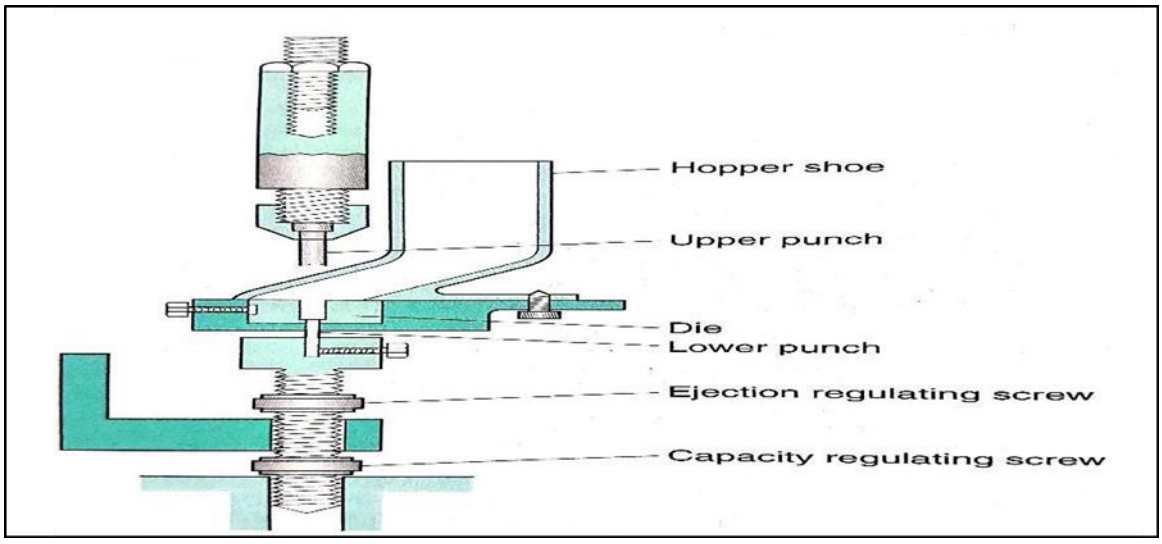


Fig.3. A single punch tablet press.

A- Feed frame, B- Die, C- Pull down cam, D- Wipe off blade, E- Weight control cam, F –Lower compression roll, G- Upper compression roll, H- Rising cam, I- Rideup cam Tablet machine **output** is regulated by three basic characteristic like:-
No of tooling sets No of compression station Rotational speed of press.
Rotary presses are engineered for fast & economical production of all kind of tablet.

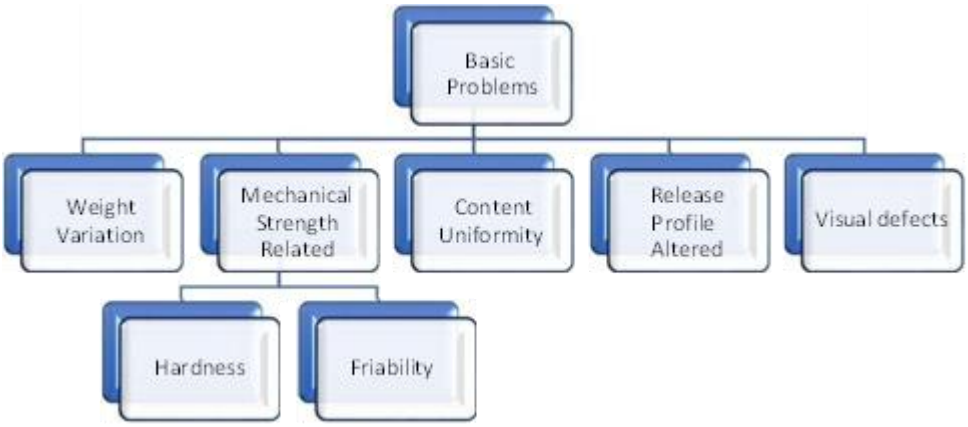
Special type machine: -

Fette machine- Chill the compression (For low MP substance like wax)

Versa press- For multi-layer tablet

Tablet Processing Problems and its remedies-

An ideal tablet should be free from any visual defect or functional defect. With the development of technology, the production process had become more simplified and more mechanized. But now the tablet punching machines are all mechanized, the mechanical feeding of feed from the hopper into the die, electronic monitoring of the press, but tablet process problem still persists. An industrial pharmacist usually encounters number of problems during manufacturing. Majority of visual defects are due to inadequate quality or inadequate moisture in the granules
ready for compression or due to faulty machine setting. Functional defects are due to faulty formulation.

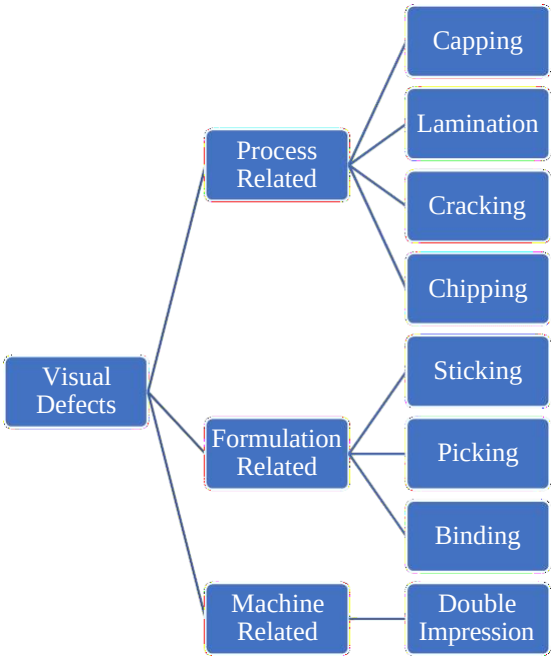


The **Imperfections** known as: 'VISUAL DEFECTS' are either related toImperfections in anyone or more of the following factors:

I. Formulation design

II. Tableting process

III. Machine



1. Capping and Lamination

Capping is the partial or complete separation of the top or bottom crowns of atablet from the main body of the tablet.

Lamination is the separation of tablet into two or more distinct layers. Usually these problems are apparent immediately after compression, or even hour or dayslater.

Detection: Subjecting tablets to the friability test is the quickest way to revealsuch problems.

Reason and Remedies

a) **Reason:** Entrapment of excess air in the granules during compression. If thegranules are light and fluffy this type of problems are encountered frequently.

Remedies: Increasing the density of granules by adding more binder orchanging the solvent of binder.

(b) **Reason:** New set of punches and dies are very tightly fitted; i.e. the clearanceis very negligible hence air cannot come out.

Remedy: In that case punch diameter should be reduced by 0.005" (i.e. 5 thou)

(c) **Reason:** Granules should not be completely dried. if over dried or underdried then capping may take place.

Remedy: So, moisture content should be kept within 1 – 4%.

Reason: Tooling set used for longer period of time will form claw-shaped curve on tipof the punch or wear ring in die in compression area – this form capping.

Remedy: Punches and dies are changed.

Picking and Sticking

Picking: -When some portion of the surface of the tablet is removed – it is termed aspicking.

Sticking: - Sticking refers to tablet materials adhering to the die wall. Serious stickingat ejection cause chipping.

Causes and Remedies of picking

Cause: When punch tips have engraving or embossing, usually of letters B, A, O aredifficult to manufacture cleanly. These may produce picking.

Remedy:

Lettering should be designed as large as possible, particularly on punches of small diameter. Plating of the punch faces with chromium produces smooth, non-adherent face. Colloidal Silica (Cab-o-sill) is added as polishing agent that makes the punch faces smooth; so that material does not cling to them.

Causes and Remedies of Sticking

***Causes*:** Excessive moisture may be responsible for sticking.

***Remedy*:** Further drying of the granulation is then required.

- During compression heat is generated and

(a) low m.p. lubricants e.g., **stearic acid** may produce sticking.

***Remedy*:** Low melting point lubricant are replaced with high melting point lubricants(e.g., **Polyethylene glycol**)

(b) Low m.p. substances, either active ingredients or additives may soften sufficientlyform the heat of compression to cause sticking.

Remedies:

- Dilution of active ingredient with additional high m.p. diluents.
- Increase in the size of tablet.
- If a low m.p. medicament is present in high concentration then refrigeration of the granules and then compressing may be the order or using fette compression machine.

2. Mottling

Mottling is an unequal distribution of color on a tablet, with light or darkpatches in an otherwise uniform surface.

***Cause*:** Migration of water-soluble dyes to the surface while drying.

Remedies:

- Change the solvent system and change the binder system
- Reduce the drying temperature
- Grind to a smaller particle size.
- Use lakes instead of water-soluble dyes.

Quality Control Tests for Tablets

General appearance: - Size, shape, and thickness: This is important to facilitatepackaging and to decide which tablet compressing machine to use.

Organoleptic properties: which include color, odor and taste of the tablets.

Weight uniformity and Content uniformity: The tablet should contain the correctdose of the drug.

Dissolution test: Drug should be released from tablet in a controlled and reproducibleway.

Weight variation, thickness & diameter: The appearance of tablet should be elegant& its weight, size & appearance should be consistent.

Hardness & friability: The tablet should show sufficient mechanical strength towithstand fracture & erosion during manufacture & handling. These factors must be controlled during production and verified after production, hence called In-process control

Official Standards as per I.P.Uncoated tablet:
Uniformity of container content and Content of active ingredient.Uniformity of weight and Uniformity of content.
Disintegration test.

Enteric coated tablet:

Disintegration test.

Dispersible tablet:

Uniformity of dispersion.Disintegration test.

Soluble tablet:

Disintegration test.

Effervescent tablet: Disintegration/Dissolution/Dispersion test.

Weight Variation

This test is based on the fact that, if the weight variation is within the limits, then it can be said that the amount of medicament will uniform considerably. Conversely, if the weight variation is not in limits, then it can be concluded that the active medicament will ununiform considerably**.**

Sources of weight variation

Weight variation is solely dependent on the poor flow property of granules and filling of die cavity. Poor flow properties arise from: (a) improper lubrication, (b) size of granules and

Weight variation test

The U.S.P. weight variation test is run by weighing 20 tablets individually, calculating the average weight, and comparing the individual tablet weights to the average. The tablets meet the USP test if "*not more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit."*

2) Content Uniformity test

Weight variation test is applicable when the amount of medicament in the tablet ishigh.

In potent drug the medicament is less in amount in comparison to the other excipients.The weight variation may meet the pharmacopoeia limitation but this will not ensure the correct variation of potency. hence, in this case the weight variation test is followedby content uniformity test.

In this test 30 tablets are randomly selected for sample, and at least 10 of them areassayed individually according to the official assay method.

9 of the 10 tablets must have potency within □ 15 % of the labelled drug content. Only1 tablet may be within □ 25%.

If this condition is not met then the tablets remaining from the 30 must be assayedindividually and none may fall outside □ 15% of the labeled content.

Disintegration Test of Tablets

The time a tablet takes to disintegrate is the disintegration time.

To test the disintegration time one tablet is placed in each tube, and the basket rack assembly is positioned in a 1-litre beaker of water, simulated gastric fluid or simulatedintestinal fluid, **at 37^0C□2^0C**, such that the tablet remains 2.5 cm from the bottom of the beaker.

A standard motor moves the basket up and down through a distance of 5 to 6 cm at a frequency of **28 to 32 cpm** (cycles per minute).

Dissolution Test

Disintegration test simply identifies the time required for the tablet to break up underthe condition of the test but it does not ensure the drug release in the bulk of the fluid.

Rate of dissolution is directly related to the efficacy of the drug. Rate of dissolution isa good index for comparing the bioavailability of two tablet products of the same drug.

Apparatus-I (Basket)

In general, a single tablet is placed in a small wire mesh basket and immersed in the dissolution medium (as specified in the monograph) contained in a **1000 ml** flask at **37^0 □ 0.5^0C.** Generally, it is rotated at **50 rpm** unless otherwise specified.

Apparatus-2 (Paddle)

The same equipment is used. Instead of basket a paddle is introduced as the stirringelement. The tablet is allowed to sink at the bottom of the flask before stirring.

Method

A tablet is taken between the 2nd and 3rd finger and pressing it with the thumb as fulcrum. If the tablet breaks with a "sharp snap", yet, it does not break when it falls onthe floor – is said to possess proper hardness.

Instruments used:

a) Monsanto Hardness Tester

b) Strong Cobb Hardness Tester -Manual mode.

c) Pfizer Hardness Tester.

d) Erweka Hardness tester. – Automatic.

e) Schleuniger Apparatus. – Operates without manual involvement.

Hardness of a tablet:

The hardness at which the tablet crushes is the hardness of the tablet.

Unit of hardness: Kg/sq.in. or lb/ sq.in
Limit: Generally maximum 5 kg/sq.in. hardness is required.

3) Friability

Tablet hardness is not an absolute indicator of strength since some formulations, when compressed into very hard tablets may produce chipping, capping and lamination problems. Therefore, another measure of tablet strength i.e. friability is often measured, i.e. the friability.

Instrument: Roche Friabilator

Objective of friability test:

This apparatus is designed to evaluate the ability of the tablet to withstand abrasion, in handling, packaging and shipping operation.

Method: 20 tablets, previously weighed are taken in the plastic chamber of the laboratory friability tester. In the plastic chamber the tablets are subjected to abrasion and shock by rotating the plastic chamber at 25 rpm for 4 mins (i.e. total 100 revolutions). The tablets are dedusted and reweighed.

Limit: - For conventional compressed tablet the weight loss should be within 0.5 to1.0 %.

Tablets Coating

Reasons Behind Coating of Tablets:

To mask the taste, odor or color of the drug. Improving the product appearance, particularly where there are visible differences in tablet core ingredients from batch to batch.

Provide physical protection, facilitates handling, particularly in high speed packaging /filling lines. Erweka Hardness tester

To provide chemical protection from its surrounding environment (particularly air, moisture and light).

To control the release of drug from the tablet e.g., sustained release tablets, repeat actiontablets.

To protect the drug from the gastric environment of the stomach with an acid resistantenteric coating.

Components Considered in Tablet Coating Tablet Properties: -

Shape,Tolerance, Surface area.
Tablet to be coated must possess the proper physical characteristics like spherical shapeand uniform surface.

To tolerate attrition of tablets during coating process they must be resistant to abrasionand chipping.

As the tablet surfaces that are brittle and soften in presence of heat or effected by coating composition and tend to become rough in

the early stages of coating process are unacceptable for film coating.

Coating process: -

A. Coating equipment

B. Coating parameters.

C. Facility & ancillary equipment.

D. Automation of coating process.

Coating composition: - which involves polymers, color, plasticizer, solvent.

Types of Coating-

(A) Sugar Coating.

Sealing-

Objectives- (i) To prevent moisture penetration into the tablet core, a seal coat is applied and (ii) To strengthen the tablet core without a seal coat, the over wetted tablets would absorb excess moisture, leading to tablet softening, and may affect the physical and chemical stability.

Ingredients

Alcoholic solutions of Shellac (10 – 30% solid) or alcoholic solution of zein,

Alcoholic solution of cellulose acetate phthalate (CAP) or alcoholic solution ofpolyvinyl acetate phthalate.

Sub-coating-

Objectives-To round the edges and build up the tablet size. Sugar coating can increase the tablet weight by 50 to 100% at this step.

Method: - The sub-coating step consists of alternately applying a sticky binder solutionto the tablets followed by a dusting of sub-coating powders and then drying. Subsequent coatings are applied in the same manner until the tablet edges have been covered and the desired thickness is achieved.

Smoothing (Syruping)-

Objectives-To cover and fill in the imperfections in the tablet surface caused by the sub- coating step.

Ingredients-Simple syrup solution (approximately 60–70%(w/w)). Often the smoothing syrups contain a low percentage of titanium dioxide (1–5%) as an opacifier.This gives a very bright and reflective background for the subsequent coloring step.

Color coating-

Objective-To impart an elegant and uniform color.
Ingredient-Syrup (60 – 70% sucrose) containing the desired color.

Method-Syrup solutions containing the dyes are coated up to 60 individual applications until the desired color is achieved. After each application of color, the coatings are dried. In the finishing step a few clear coats of syrup may be applied.

Polishing-

Objective-To produce the desired luster on the surface of the tablet.
Ingredients-Mixtures of waxes (like beeswax, carnauba wax, candela wax or hardparaffin).

Method-Either this mixture of waxes is applied as powder or as dispersions in variousorganic solvents in a polishing pan (canvas line pan).

Printing-In order to identify sugar-coated tablets often it is necessary to print them,using pharmaceutical grade ink, by means of a process of offset rotogravure.

(B) Film Coating

Film coating adds 2 to 5% to the tablet weight. Film coating is a complex process thatinvolves the application of thin (in the range of 20-200 μm) polymer-based coatings toan appropriate substrate (tablets, pellets, granules, capsules, powders, and crystals) under

conditions that permit:

1. Balance between (and control of) the coating liquid, addition rate and dryingprocess.
2. Uniformity of distribution of the coating liquid across the surface of productbeing coated.
3. Optimization of the quality (both visual and functional) of the final coatedproduct.

Advantage-

- Substantial reduction in quantity of coating applied (2-4% for film coating,compared with 50-100% for sugar coating).
- Faster processing times and Improvement in process efficiency and output.
- Greater flexibility in optimizing formulations as a result of the availability ofa wide range of coating materials and systems.
- Ability to be applied a wide range of pharmaceutical products.

Types

1) Pan-pour method-

Viscous coating materials are directly added from some container into the rotating panmoving with the tablet bed. Tablets are subjected to alternate solution application, mixing and then drying.

Disadvantages:

The method is relatively slow and it relies heavily on the skill of the operator.

- Tablets always require additional drying to remove the latent solvent.
- Aqueous film coating is not suitable for this method because localized overwetting will produce physicochemical instability.

2) Pan-spray method-

Coating material is sprayed over the tablet bed from nozzles and hot air is passed through the tablet bed to dry it. The variables to be controlled is pan-spray film coating process are:

(a) Pan variables:

Uniform mixing is essential to deposit the same quantity of film on each tablet.

1. *Pan design or baffling*: Some tablet shapes mixes freely while other shapes mayrequire a specific baffling arrangement to ensure adequate mixing.

Disadvantages: Baffles may produce chipping and breakage if not selected properly.

(b) Pan speed

- Pan speed affects mixing and the velocity at which the tablet pass under thespray.
- Too slow speed cause localized over-wetting resulting in tablets sticking toeach other or to the pan.
- Too high speeds may not allow enough time for drying before the same tablets are reintroduced to the spray. This results in a rough coating appearanceon the tablets.

Optimum pan speed: 10 – 15 rpm for nonaqueous film coating.

3 – 10 rpm for aqueous film coating

3) Fluidized bed process (air suspension coating)

This process have been successfully used for rapid coating of tablets, granules and capsules. Process variables are as follows: (a)

Chamber design and air flow rate control the fluidization pattern, (b) Tablet shape, size and density, (c) Volume and rateof air flow either too high rate produce attrition and breakage of tablets or too low rate
 mass does not move fast enough through the spray region over-wetting occursand (d) Inlet and exhaust air temperature.

Examples-

Non-enteric materials: e.g., Hydroxypropyl methylcellulose (HPMC), Methylhydroxy ethyl cellulose (MHEC), Ethyl cellulose (EC), Polyvinyl pyrrolidone (PVP), Sodium carboxymethyl cellulose (Sod. CMC), Polyethylene glycols (PEG), Acrylate polymers e.g., Eudragit E

Enteric materials: e.g., Cellulose acetate phthalate (CAP), Acrylate polymers (Eudragit L, S), Hydroxypropyl methylcellulose phthalate (HPMCP), Polyvinyl acetate phthalate (PVAP).

(c) Spray variables

1) Rate of liquid application.

2) Spray pattern.

3) Degree of atomization

These three spray variables are interdependent. For spraying two types of systems are there:
(a) High-pressure, airless system and (b) low-pressure, air atomization system.

(d) Process air variables (temperature, volume, rate) are required for optimum drying of the coating by evaporation of the solvent. The balance between the supply and exhaust air flow should be such that all the dust and solvent are confined within the coating system

(C) Enteric Coating

1) Pan-pour method.
2) Pan-spray method.
3) Fluidized bed process (air suspension coating)

CONCLUSION

As a solid dosage form, tablets are popular among patients and practitioners alike as they provide a means of self-administration. The formulation of a tablet contains, in addition to the API, various substances to assure proper delivery of the API to the patient. With advancement in technology and increase in awareness towards modification in standard tablet to achieve better acceptability as well as bioavailability,newer and more efficient tablet dosage forms are being developed. The main reasons behind formulation of different types of tablets are to create a delivery system that is relatively simple and inexpensive to manufacture. Provide the dosage form that is convenient from patient's perspective and utilize an approach that is unlikely to add complexity during regulatory approval process. To understand each dosage form,tablets here are classified by their route of administration and by the type of drug delivery system they represent within that route.

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