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Tablets

They are the pharmaceutical oral solid dosage form . They are fornulated either by molding and compression. They vary in shape, size and weight depending on the medicinal substances .

Advantages

1.Least content variability
2.Light and compact
3.Easy and cheap to package
4.Easy to carry
5.Sustained release product is possible by various techniques.
6.Suitable for large scale production.
7.Product identification is easy.

Disadvantages

1.Difficult to swallow in case of children and unconcious patient.
2.Drugs with poor wetting , slow dissolution properties may be difficult to formulate .
3.Bitter tasting drugs , drugs with an obejctionable odour may require coating or encapsulation.

Classification of tablets

1. **Orally ingested tablets**
    - compressed tablets e.g Paracetamol
    - Multi compressed tablets
    - Delayed release tablets e.g Enteric coated tablets
    - Sugar coated tablets e.g Multivitamin tablets
    - Film coated tablets e.g Metronidazole tablets
    - Chewable tablets e.g Antacid tablets

2. **Used in oral cavity**
    - Buccal tablet e.g Vitamin C tablet
    - Sublingual tablet e. g Vicks Menthol tablet
    - Troches or lozenges
    - Dental cone

3. **Other route**
    - Implantation tablet
    - Suppositories or insert e.g Clotrimazole tablet

4.Used to prepare solution
- Effervescent tablet e .g Disprin
- Dispensing tablet e.g Enzyme tablet(Digiplex)
- Hypodermic tablet

Excipients

An excipient is a substance formulated alongside the active ingredient of a medication, included for the purpose of long-term stabilization, bulking up solid formulations that contain potent active ingredients in small amounts (thus often referred to as "bulking agents", "fillers", or "diluents"), or to confer a therapeutic enhancement on the active ingredient in the final dosage form, such as facilitating drug absorption, reducing viscosity, or enhancing solubility. Excipients can also be useful in the manufacturing process, to aid in the handling of the active substance concerns such as by facilitating powder flowability or non-stick properties, in addition to aiding in vitro stability such as prevention of denaturation or aggregation over the expected shelf life. The selection of appropriate excipients also depends upon the route of administration and the dosage form, as well as the active ingredient and other factors. A comprehensive classification system based on structure-property-application relationships has been proposed for excipients used in parenteral medications.

Types

Antiadherents

Antiadherents reduce the adhesion between the powder (granules) and the punch faces and thus prevent sticking to tablet punches by offering a non-stick surface. They are also used to help protect tablets from sticking. The most commonly used is magnesium stearate.

Binders

Binders hold the ingredients in a tablet together. Binders ensure that tablets and granules can be formed with required mechanical strength, and give volume to low active dose tablets. Binders are usually:

Saccharides and their derivatives:
Disaccharides: sucrose, lactose;
Polysaccharides and their derivatives: starches, cellulose or modified cellulose such as microcrystalline cellulose and cellulose ethers such as hydroxypropyl cellulose (HPC);
Sugar alcohols such as xylitol, sorbitol or mannitol;
Protein: gelatin;
Synthetic polymers: polyvinylpyrrolidone (PVP), polyethylene glycol (PEG)...
Binders are classified according to their application:

Solution binders are dissolved in a solvent (for example water or alcohol can be used in wet granulation processes). Examples include gelatin, cellulose, cellulose derivatives, polyvinylpyrrolidone, starch, sucrose and polyethylene glycol.
Dry binders are added to the powder blend, either after a wet granulation step, or as part of a direct powder compression (DC) formula. Examples include cellulose, methyl cellulose, polyvinylpyrrolidone and polyethylene glycol.

Coatings

Tablet coatings protect tablet ingredients from deterioration by moisture in the air and make large or unpleasant-tasting tablets easier to swallow. For most coated tablets, a cellulose ether hydroxypropyl methylcellulose (HPMC) film coating is used which is free of sugar and potential allergens. Occasionally, other coating materials are used, for example synthetic polymers, shellac, corn protein zein or other polysaccharides. Capsules are coated with gelatin.

Enterics control the rate of drug release and determine where the drug will be released in the digestive tract. Materials used for enteric coatings include fatty acids, waxes, shellac, plastics, and plant fibers.

Colors

Colors are added to improve the appearance of a formulation. Color consistency is important as it allows easy identification of a medication. Furthermore, colors often improve the aesthetic look and feel of medications. Small amounts of coloring agents are easily processed by the body, although rare reactions are known, notably to tartrazine.Commonly, titanium oxide is used as a coloring agent to produce the popular opaque colors along with azo dyes for other colors. By increasing these organoleptic properties a patient is more likely to adhere to their schedule and therapeutic objectives will also have a better outcome for the patient especially children.

Disintegrants

Disintegrants expand and dissolve when wet causing the tablet to break apart in the digestive tract, or in specific segments of the digestion process, releasing the active ingredients for

absorption. They ensure that when the tablet is in contact with water, it rapidly breaks down into smaller fragments, facilitating dissolution.

Examples of disintegrants include:

Crosslinked polymers: crosslinked polyvinylpyrrolidone (crospovidone), crosslinked sodium carboxymethyl cellulose (croscarmellose sodium).
The modified starch sodium starch glycolate.

Flavors

can be used to mask unpleasant tasting active ingredients and improve the acceptance that the patient will complete a course of medication. Flavorings may be natural (e.g. fruit extract) or artificial.

For example, to improve:

a bitter product - mint, cherry or anise may be used
a salty product - peach, apricot or liquorice may be used
a sour product - raspberry or liquorice may be used
an excessively sweet product - vanilla may be used

Glidants

Glidants are used to promote powder flow by reducing interparticle friction and cohesion. These are used in combination with lubricants as they have no ability to reduce wall friction. Examples include silica gel, fumed silica, talc, and magnesium carbonate. However, some silica gel Glidants such as Syloid(R) 244 FP and Syloid(R) XDP are multi-functional and offer several other performance benefits in addition to reducing interparticle friction including moisture resistance, taste marketing etc.

Lubricants

Lubricants prevent ingredients from clumping together and from sticking to the tablet punches or capsule filling machine. Lubricants also ensure that tablet formation and ejection can occur with low friction between the solid and die wall.

Common minerals like talc or silica, and fats, e.g. vegetable stearin, magnesium stearate or stearic acid are the most frequently used lubricants in tablets or hard gelatin capsules.
Lubricants are agents added in small quantities to tablet and capsule formulations to improve certain processing characteristics. While lubricants are often added to improve manufacturability of the drug products, it may also negatively impact the product quality.

There are three roles identified with lubricants as follows:

True lubricant role:
To decrease friction at the interface between a tablet's surface and the die wall during ejection and reduce wear on punches & dies.
Anti-adherent role:
Prevent sticking to punch faces or in the case of encapsulation, lubricants
Prevent sticking to machine dosators, tamping pins, etc.

Glidant role:
Enhance product flow by reducing interparticulate friction.

There are two major types of lubricants:

Hydrophilic
Generally poor lubricants, no glidant or anti-adherent properties.
Hydrophobic
Most widely used lubricants in use today are of the hydrophobic category. Hydrophobic lubricants are generally good lubricants and are usually effective at relatively low concentrations. Many also have both anti-adherent and glidant properties. For these reasons, hydrophobic lubricants are used much more frequently than hydrophilic compounds. Examples include magnesium stearate.

Preservatives

Some typical preservatives used in pharmaceutical formulations are

Antioxidants like vitamin A, vitamin E, vitamin C, retinyl palmitate, and selenium
The amino acids cysteine and methionine
Citric acid and sodium citrate
Synthetic preservatives like the parabens: methyl paraben and propyl paraben.

Sorbents

Sorbents are used for tablet/capsule moisture-proofing by limited fluid sorbing (taking up of a liquid or a gas either by adsorption or by absorption) in a dry state. For example, desiccants absorb water, drying out (desiccating) the surrounding materials.

Sweeteners

Sweeteners are added to make the ingredients more palatable, especially in chewable tablets such as antacid or liquids like cough syrup. Sugar can be used to mask unpleasant tastes or

smells, but articificial sweeteners tend to be preferred, as natural ones tend to cause tooth decay.

Vehicles

In liquid and gel formulations, the bulk excipient that serves as a medium for conveying the active ingredient is usually called the vehicle. Petrolatum, dimethyl sulfoxide and mineral oil are common vehicles.

Formulation of tablets

In the tablet pressing process, the appropriate amount of active ingredient must be in each tablet. Hence, all the ingredients should be well-mixed. If a sufficiently homogenous mix of the components cannot be obtained with simple blending processes, the ingredients must be granulated prior to compression to assure an even distribution of the active compound in the final tablet. Two basic techniques are used to granulate powders for compression into a tablet: wet granulation and dry granulation. Powders that can be mixed well do not require granulation and can be compressed into tablets through direct compression.

Wet granulation

Wet granulation is a process of using a liquid binder to lightly agglomerate the powder mixture. The amount of liquid has to be properly controlled, as over-wetting will cause the granules to be too hard and under-wetting will cause them to be too soft and friable. Aqueous solutions have the advantage of being safer to deal with than solvent-based systems but may not be suitable for drugs which are degraded by hydrolysis.

Procedure

1.The active ingredient and excipients are weighed and mixed.

2.The wet granulate is prepared by adding the liquid binder–adhesive to the powder blend and mixing thoroughly. Examples of binders/adhesives include aqueous preparations of cornstarch, natural gums such as acacia, cellulose derivatives such as methyl cellulose, gelatin, and povidone.

3.Screening the damp mass through a mesh to form pellets or granules.

4.Drying the granulation. A conventional tray-dryer or fluid-bed dryer are most commonly used.

5.After the granules are dried, they are passed through a screen of smaller size than the one used for the wet mass to create granules of uniform size.

Low shear wet granulation processes use very simple mixing equipment, and can take a considerable time to achieve a uniformly mixed state. High shear wet granulation processes use equipment that mixes the powder and liquid at a very fast rate, and thus speeds up the manufacturing process. Fluid bed granulation is a multiple-step wet granulation process performed in the same vessel to pre-heat, granulate, and dry the powders. It is used because it allows close control of the granulation process.

Dry granulation

Dry granulation processes create granules by light compaction of the powder blend under low pressures. The compacts so-formed are broken up gently to produce granules (agglomerates). This process is often used when the product to be granulated is sensitive to moisture and heat. Dry granulation can be conducted on a tablet press using slugging tooling or on a roll press called a roller compactor. Dry granulation equipment offers a wide range of pressures to attain proper densification and granule formation. Dry granulation is simpler than wet granulation, therefore the cost is reduced. However, dry granulation often produces a higher percentage of fine granules, which can compromise the quality or create yield problems for the tablet. Dry granulation requires drugs or excipients with cohesive properties, and a 'dry binder' may need to be added to the formulation to facilitate the formation of granules.

Tablet compression and processing problems

Tablet defects occur for a variety of reasons, but many can easily be avoided. To address defects, technicians involved in tabletting must have a full understanding of both the tabletting process and the materials used. Adequate training in the setting up and use of the machines is vital if the technician is to have the necessary skills to be able to fix equipment and minimize problems in production. A professional and experienced technician can turn an ordinary product into a high quality one whereas a novice or inexperienced operator cannot, and might even be afraid to adjust the machine in order to prevent or correct problems. When the equipment is properly operated the tablet production will go smoothly.

Problems such as tablet defects can cause the company loss of production time and sales, and therefore money. Common problems that afflict the tabletting industry include:

Weight variation
Friability
Hardness
Sticking
Picking
Capping
Laminating
Chipping
Mottling

Double press or impression

Although there are several defects that affect the tablet making process, capping/laminating, hardness and sticking/picking are the three most commonly encountered.

These defects usually arise from:

Problems with the unit upstream
Problems with the tablet press
Poor quality raw materials
Defects caused by the formulation
Milling process causes too many fines that result to capping, hardness, lamination and black spots
Failure of compression
Poor flow and compressibility of the powder
Product is too dry or too wet preventing proper ejection

Below are the three common defects and how best to avoid them.

Capping

Capping happens when a fracture occurs at the top of the tablet and the top, or cap, separates itself from the body of the solid tablet. It is often caused by air trapped in the powder material during the compression stage. It can also arise because the press fails to compress the formulation due to the collection of powder fines.

When a tablet is compressed air is expelled from the powder granules allowing each of the particles to stick together. The press is designed to allow the air to dissipate during the compression process. As the air is released from the granules it can also push very fine dry granules fines outwards. These particles generally do not stick together and when the particles are pushed into the line of air being released near the cup and the tablet band, the fines prevent the granules from being compressed resulting in the tablet becoming fractured.

As the air is released when the upper punch die tip is raised, capping only occurs at the top of the tablet. If a fracture occurs in the lower part of the tablet, it is referred to as lamination, and is discussed below.

The faster the press speed, the more likely it is that capping will occur and simply reducing the speed of the press will often solve the problem. That said, there are other ways that this problem may be solved.

Poor formulation as well as bad processing practice can often cause capping. Dry blends can cause capping, as a low moisture content of the formulation tends to prevent the particles from

blending with each another. The binder, which is added to a formulation to help bind the particles together, may not be adequate for the particular materials. In the event that capping does occur, it is therefore worthwhile reviewing the choice of binder. Improper mixing or blending can add air to the formulation, and inadequate mixing can also cause powders to segregate, leading to tablet capping. Over blending can itself cause problems so careful optimization of the blending process is required to ensure consistent quality of tablet production.

Capping is usually easy to fix either by increasing the dwell time (i.e., slowing down the production) or by careful analysis of the formulation and production process.

Lamination

Lamination is the term used for a split in the tablet anywhere but at the top. Lamination is essentially the same as capping and with similar causes. It is, nevertheless, important to diagnose the lamination issue correctly to ensure that proper steps are taken to solve the problem. Lamination often occurs due to the over compression of the tablet. Too much compression can lead to the granules flattening out and thus preventing them from locking together. This can also happen when light or fine particles do not combine, as these particles do not compress well. To prevent this, the thickness of the tablet needs to be reduced, and/or the dwell time increased to allow the fine particles to combine. To increase dwell time, pre-compression can be employed or the speed of the tablet machine can be reduced. Another option is to use a tapered die rather than a perfectly cylindrical die bore. Tapered dies generally do not exhibit capping or laminating problems.

Steps in Eliminating Capping/Laminating

1.Punch Penetration. Check if the tablet press has an adjustable punch penetration. Adjusting the upper punch penetration depth in the die can allow better air exhaust, which can often solve the issue quickly. The punch penetration setting for pre-compression penetration does not have to be the same as for the main compression step.

2.Pre-compression. New models of high-speed rotary tablet press incorporate pre compression, which is an initial compression step before the main compaction step. Pre-compression is a means of compact the powder but at a lighter pressure than the main compression step. It is used especially if there are dry dust fines or particles – it binds the particles together using a lighter force, so that they cannot migrate out during the final compression step. If the tablet needs more dwelling time, pre-compression can be done twice with a higher force the second pre-compression step.

3.Slow the Press Down. By decreasing the speed of the press, the dwell time or the time that the tablet is under pressure is increased. By slowing the press and extending the dwell time, air is allowed to evacuate, giving the particles time to bind themselves to each other, leading to a controlled hardness once tablets are released. It is important, however, to make sure that the

dwell time is not too long as that may lead to particles becoming too dry and the tablets laminating. Clearly extending dwell time is one method of solving the capping issue but it needs to be managed so that it does not introduce a laminating issue.

4.Tooling Design. The design of the tablet tooling can influence capping and laminating. A dome headed tool can extend dwelling time and changing the cup depth and radius can help make air release faster during compression stage. Additionally, adding a taper to the die can help evacuate trapped air during compression and reduce the tendency of the tablet to cap. Tapering can also reduce the force that contributes to the tablets' tendency to laminate. Remember that proper care and maintenance can eliminate other problems such as j-hook, compression wear rings within the die and premature punch tip wear.

Equipments and tablet tooling

1. **Rapid mixer granulator(RMG)**

It is a multipurpose processor equally suitable for high speed dispersion of dry powders, aqueous or solvent granulations and mixing purposes.

Working and principle :

1.Mixing and wet granulation process is performed in one sequence.

2.The fast moving mixer blades enforce the powder material into the spiral fluidization at the bowl base

3.This vortex effect in the material provides faster and uniform distribution of the ingredients.

4.This intensive mixing action distributes active substances homogeneously within few minutes.

5.By adding binder through charging hole at the top cover particles are uniformly moistened and aggregated to large granules.
6.The vertically rotating, specially designed chopper blades shears the circulating powder and breaks down lumps and aggregates .

7.Thus granules attain higher density and uniformity in shape, thereby achieving a uniform particle size distribution