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A Review on Solid Dosage form: Tablet

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Abstract

Review Article

Tablet is defined as solid pharmaceutical dosage form containing drug substance generally with suitable diluents and prepared by either compression or molding methods. Tablets remain popular as a dosage form because of the advantages afforded, both to the manufacturer (e.g. simplicity and economy of the preparation, stability, and convenience in packing, shipping and dispensing) and the patient. Because of their composition, method of manufacture or intended use, tablets present a variety of characteristics and consequently there are several categories of tablets. Tablet formulation and design may be described as the process whereby the formulator ensures that the correct amount of the drug in the right form is delivered at or over the proper time at the proper rate and in the desired location, while having its chemical integrity protected to that point. Latest concepts and regulations focus on bioavailability, bioequivalence and validation etc. impact formulation designing and manufacture.

Keywords: Tablet, Solid pharmaceutical dosage form, Compression or molding methods.

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1. INTRODUCTION

1.1 Tablet [1]

Tablets have been used since later part of 19th century. Tablets are solid unit dosage form of medicaments with or without suitable diluents and prepared either by molding or compression. They are very greatly in shape, size and weight which depend upon amount of medicament used and mode of administration. Usually they are disc, flat or biconvex in shape. They also vary in hardness, thickness, disintegration and dissolution characteristic and in other aspect depending upon their intended use and method of manufacture. Tablets are the most widely used solid dosage form of medicament. Because of their advantages, their popularity is increased day by day, and ruling the world.

1.1.1 Properties of an ideal tablet [2]

- The objective of formulation and fabrication of the tablet is to deliver the exact amount of drug in proper form at predicted over proper time and at proper target.
- Tablet should be elegant having its own identity and free from defect such as crack, chips, contamination and decoloration etc.

- It should have chemical and physical stability to maintain its physical integrity over time.
- It should be capable to prevent and alteration in the chemical and physical properties of medicaments agents.
- It should be capable of withstanding of rigor of mechanical shocks encountered in its production, packing, shipping and dispensing.
- An ideal tablet should be able to release the medicaments in body in predictable and reproducible manner.

Advantages [3]

- Tablets are unit dosage form those provide an accurate, stable dose with greatest precision and least content variability.
- Tablets are easy to use, handle and carry by the patients.
- Tablets are attractive and elegant in appearance.
- Tablets are most stable dosage form with respect to their physical, chemical and micro biological attributes.
- The manufacturing cost of tablet is low as compared to other dosage form and their manufacturing speed is also quite high.

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- The packing and shipping of tablet is comparatively easy and cheap.
- The unpleasant taste and odour of medicaments can be easily masked by sugar coating.
- The incompatibility of medicaments and their deterioration due to environmental factor are less in case of tablets.
- They are more suitable for large scale production then other oral dosage forms.
- Tablets provide administration of even minute dosage of drug in an accurate amount.
- Their identification is probably the easiest because of variety of shape and colour.
- Tablets are formulated with certain special release profile product such as enteric and delayed release product [3].

Table 1.1: Various type of tablet used in different route											
	T T		-	• •			• •			T 7	

Tablet			
Oral for ingestion	Used in oral cavity	Administered by other route	Used to prepare solution
Compressed tablet	Buccal tablet	Implantation tablet	Efferv escent tablet
Multiple compressed tablet	Sublingual tablet	Vaginal tablet	Dispensing tablet
Delayed action tablet	Troches and Lozenges		Hypodermic tablet
Sugar coated	Dental cone		Tablet triturate
Film coated tablet			
Chewable tablet			

1.1.2 Excipients are commonly used in tablets and has following functions, as [4]

• Diluents

Tablet

- Binders
- Lubricants
- Glidants
- Disintegrates

• Colouring and flavouring agents

1.1.2.1 Diluents

The amount of API is not sufficient for compression so inert substances are used to add for bulk to make the tablet a practical size for compression. Those inert substances are known as Diluents.

Table 1.2: Common Tablet Diluents	5
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Diluents	Comments			
Lactose	Available as anhydrous and monohydrate. Anhydrous material used for direct			
	compression due to superior compressibility.			
Microcrystalline cellulose Originally a direct compression excipient, now often included in granulations due				
	excellent compressibility.			
Dextrose, glucose	Direct compression diluent, often used in chewable tablets			
Sucrose	Was widely used as a sweetener/filler in effervescent tablets and chewable tablets. Less			
	popular nowadays due to cariogenicity.			
Starch and derivatives	Versatile material can be used as diluent binder and disintegrant.			
Calcium carbonate	Brittle material			
Dicalcium phosphate	Excellent flow properties. Brittle material.			
Magnesium carbonate	Direct compression diluent.			

1.1.2.2 Binder

Binder is one of an important excipient to be added in tablet formulation. In simple words, binders or

adhesives are the substances that promote cohesiveness. It is utilized for converting powder into granules through a process known as granulation.

Binder	Normal usage	Comments
	concentration (%)	
Starch	5–25	Was once the most commonly used binder. The starch has to be
		prepared as a paste, which is time consuming.
Pregelatinized starch	5-10	Cold water soluble, so easier to prepare than starch.
Acacia	1–5	Requires preparation of paste prior to use. Can lead to prolonged
		disintegration times if used at too high a concentration.
Polyvinylpyrrolidone (PVP)	2-8	Available in range of molecular weights. Can be added either dry
		or in solution. Soluble in water and ethanol.
Hydroxypropyl	2-8	Available in range of molecular weight. Soluble in water and
methylcellulose (HPMC)		ethanol.
Methylcellulose	1–5	Low-viscosity grades most widely used.

1.1.2.3 Lubricants

Lubricants are the substances which prevent adhesion of the tablet material to the surface of the dies and punches, reduce interparticular friction, facilitate an easy ejection of tablets from the die cavity and improves rate of flow of tablet granulation. The quantity of lubricant significantly varies from 0.1 to 5%. Commonly used lubricants are Talc, magnesium stearate, calcium stearate, stearic acid, hydrogenated vegetable oil and PEG (Polyethylene Glycol).

Туре	Example	Level	Comments
	_	required (%)	
Boundary	Magnesium stearate	0.2–2.0	Hydrophobic, variable properties between suppliers
lubricants	Calcium stearate.	0.5-4.0	Hydrophobic
	Sodium stearyl fumarate.	0.5-2.0	Less hydrophobic than metallic stearates, partially soluble
	Polyethylene glycol 4000 and 6000	2–10	Soluble, poorer lubricant activity than fatty acid ester salts.
	Sodium lauryl sulfate	1–3	Soluble, also acts as wetting agent.
	Magnesium lauryl sulfate.	1–3	Acts as wetting agent
Fluid	Light mineral oil	1–3.	Hydrophobic, can be applied to either formulation or tooling
lubricants	Hydrogenated vegetable	1–5.	Hydrophobic, used at higher concentrations as controlled-
	oils		release agents
	Stearic acid.	0.25–2	Hydrophobic
	Glyceryl behenate	0.5 - 4.0	Hydrophobic also used as controlled-release agent.

Table 1.4. hybridants and their uses

1.1.2.4 Glidants

A glidant is a substance that improves the flow char acteristics of a powder mixture. These materials are always added in the dry state just prior to compression. They are used in concentration less than 1%. Talc is also used and may serve the dual purpose of lubricant/glidant. The most commonly used glidants are colloidal silicon dioxide and asbestos free talc.

Table 1.5. Commonly Used Gudants							
Glidant	Typical percentage						
Talc	1-5						
Fumed silicon dioxide	0.1-0.5						
Starch	1-10						
Calcium silicate	0.5-2.0						
Magnesium carbonate (heavy)	1-3						
Magnesium oxide (heavy)	1-3						
Magnesium lauryl sulfate	0.2–2.0						
Sodium lauryl sulfate	0.2–2.0						

 Table 1.5: Commonly Used Glidants

1.1.2.5 Disintegrants

Disintegrants are the substance or a mixture of substances added to a tablet to facilitate its break up or disintegration after administration. Starches, clays, cellulose and cross linked polymers are most commonly used disintegrants. The oldest and still the most popular disintegrants are corn and potato starch. Other ingredients like veegum, methyl cellulose, agar, bentonite, cellulose, citrus pulp and CMC are also used. They are mostly added into two portions, one part is added prior to granulation and the remainder is mixed with the lubricant and finally both are mixed just before the compression.

Disintegrant	Normal usage	Comments	
	concentration (%)		
Starch	5-10	Probably work by wicking; swelling is minimal at body	
		temperature	
Microcrystalline cellulose		Strong wicking action. Loses disintegrant action when highly	
		compressed.	
Insoluble ion exchange resins		Strong wicking tendencies with some swelling action.	
Sodium starch glycolate	2-8	Free-flowing powder that swells rapidly on contact with water.	
Croscarmellose sodium	1–5	Swells on contact with water.	
Gums—agar, guar, xanthan	<5	Swell on contact with water; form viscous gels that can ret	
		dissolution, thus limiting concentration that can be used.	
Alginic acid, sodium alginate	4–6	Swell like the gums but form less viscous gels.	
Crospovidone	1–5	High wicking activity.	

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1.1.3 Tablet excipients must meet certain criteria in the formulation such as

- They should be non toxic and acceptable to the regulatory agencies in all countries where the product is to be marketed.
- They should be commercially available in an acceptable grade in all countries where the product is to be manufactured.
- Their cost should be acceptably low.
- They should be physiologically inert.
- They should be free of any unacceptable microbiologic load.
- They should be color compatible (not producing any off-color appearance)
- If the drug product is also classified as a food (e.g. certain vitamins products), the diluents and other exipient must be approved direct to food additives.
- They should have no deleterious effect on the bioavailability of the drug(s) in the product.

1.2 Magnesium stearate as Pharmaceutical lubricants [5-7]

Magnesium Stearate exists as "Plate-like" crystals (or lamellae) stacked together like a deck of cards. As the blending process proceeds, plates continue to shear off and coat adjacent particles of granules, drug or other excipients. The higher the concentration of Magnesium Stearate used or the longer this blending continues, the more complete this coating of the adjacent particles will become.

It has low friction coefficient and high covering potential. The lubricant efficiency and extent of surface coverage depend on the mixing time of the tablet mass with Magnesium Stearate because of its laminar structure.

Introduction of the high-speed tableting machine requires the use of higher concentrations of Magnesium Stearate, but increasing concentration of Magnesium Stearate can adversely affect the flow properties of the tableting mass and the quality properties of tablets.

Lubricant concentration were studied on the prior enumerated factors. The powders were mixed, blended to homogeneity, sheared, and compressed into tablets. Then the resulting tablets were tested for hydrophobicity, tablet hardness, tablet weight, and dissolution. It was found that including the glidant and lubricant was vital to counteract static and press adherence. However, the percentage of their concentrations must be kept at approximately 1% to avoid altering the powder and tablet properties as well as decreasing the dissolution rate.

1.2.1 Properties of lubricants [8, 9]

- A lubricant should be capable of reducing wear on rubbing surfaces.
- Lubricants are added to tablet formulation primarily to reduce friction between die wall and granules as tablet is formed and ejected.
- Prevention of sticking of granules to the tooling anti adherent.
- Improvement of granules flow property.
- Lubricants Helps tablet to easily eject from the die cavity and would prevent sticking of tablet to die cavity as well.

1.2.2 Method of addition of lubricants [10]

The lubricant is divided finely by passing it through a 60 to 100 mesh nylon cloth on to the granulation. In production this is called 'bolting the lubricant'.

After addition the granulation is tumbled or mixed gently to distribute the lubricant without coating all the particles too well.

- Complete coating will produce dissolution problem.
- Prolonged mixing will produce excessive fines by breaking the granules.

1.3 Method of Tablet Preparation [11-16]

There are three general methods of tablet preparation.

- $\clubsuit \quad \text{Wet granulation method}$
- Dry granulation method
- Direct compression method

1.3.1 Wet Granulation Method

This is the oldest and the most widely used method of tablet preparation. The powdered and mixed tablet ingredients are converted into a moist coherent mass and then into granules before compression into tablets. The essential steps that are involved during the preparation of tablet are weighing, mixing, granulation, screening the dump mass, drying, dry screening, lubrication and finally compression. This method is time consuming. The process involves the blending and mixing of active ingredients, diluents and disintegrant. The mixed material is then sifted through a screen of suitable mesh to remove or break the lumps. The sifted material is converted into a damp mass by adding and mixing with the binder solution. The damp mass is forced through 6-8 mesh screens for granulation. The wet granules are dried in an oven; particles may agglomerate and forms lumps and therefore dry screening operation is often required after drying. To the dried granules is then added the remaining quantity of disintegrant and lubricant. Finally the granules are compressed into tablets.



Figure 1: Wet Granulation

1.3.2 Dry Granulation Method

This process of granulation is also known as slugging, double Compression or recompression method. This process of tablet preparation is commonly used when the tablet ingredients are sensitive to moisture or unable to withstand elevated temperature during drying. Under such conditions dry granulation is the method of choice provided the tablet ingredients have sufficient inherent binding or cohesive properties. The essential steps are weighing, mixing, slugging, dry screening, lubrication and compression. For the formation of a cohesive slug, spray dried or powdered binders such as acacia or microcrystalline cellulose may be added to the dry powder. Lubricants are added to reduce powder adhesion to the punches and to facilitate ejection of intact slugs from the dies. Initially large slugs are obtained by compressing powdered material containing excipients. The slugs are then forced through mesh screen breaking them into granules. The remaining lubricant is added to the granulation with gentle blending and the resulting material is compressed into tablet.



Figure 2: Dry Granulation

1.3.3 Direct Compression Method

The method consists of compressing tablets directly from powdered material without modifying the physical nature of the materials itself. This method of tablet making is of special interest for small group of crystalline chemicals having the entire physical characteristic necessary for the formulation of a good tablet. Substances like chlorides, chlorates, bromides, iodides, nitrates and permanganates, salts of potassium, ammonium chloride and methanamine etc are manufactured by direct compression as they have cohesive properties. Advantages of this method are simplicity of process, absence of granulating steps, avoidance of moisture and drying step, minimum material handling, and rapidity of the total process. The limitations of this method are that only a few crystalline drugs can be directly compressed otherwise this process has no other major limitation.

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Figure 3: Direct Compression

1.4 Effect of Lubricants 1.4.1 Effact of Lubricants on Granules [17, 18]

Powder flows when gravitational forces become higher than the friction and cohesion forces that influence particle-particle interactions. Cohesive forces refer to the attraction between particles and include van der Waals' forces, capillary forces and electrostatic forces. Cohesive forces are affected by the surface properties of the particles. As boundary layer lubricants form a film around particles, these lubricants affect the cohesive forces thereby also affecting powder flow. Furthermore, friction is also affected by the surface properties of the particles. Friction acts at contact points between particles; thus, surface morphology affects friction forces. If the contact area is increased, the potential contact points are increased, thus increasing friction. Boundary layer lubricants reduce friction by reducing surface irregularities, reducing contact points between particles, and thus friction forces.

1.4.2 Effect of lubricants on tablet properties [19-21]

Besides reducing friction and cohesion, lubricants may cause undesirable changes in the properties of the tablet. The presence of lubricant in a powder is thought to interfere in a destructive way with the bonding between particles during compaction, thus reducing final tablet strength Lubricant type, concentration, method of lubrication, and the manner of incorporating the lubricant all affect the tablet compression It is generally accepted that magnesium stearate has more negative effect on the hardness and tensile strength of the tablets with more deformable materials than brittle ones the powder form of magnesium stearate have more adverse effects on tablet hardness and disintegration than the granular form.

Other lubricants, such as stearic acid and talc, showed no effect on the interparticle bonding and tablet strength. But magnesium stearate show the decrease in the magnesium stearate level from 1.7 mg to 0.85 mg in a tablet comprised of mostly calcium phosphate dibasic reduced the disintegration time from 10 to 4.5 min and showed that disintegration time increased substantially more for increases of magnesium stearate than other lubricants stearic acid and stearyl alcohol.

1.5 Tablet Compression Tooling [22-26]

The compressed tablet is the most popular dosage form in use now a day. Size of tablets to be swallowed range from a few millimeters to about centimeters. Tablets are often stamped with symbols, letters, and numbers, which enable them to be identified. Tablets can be made in virtually any shape, although requirements of patients and tableting machines mean that most are round, oval or capsule shaped. More unusual shapes are more vulnerable to chipping or manufacturing problems. Tablet diameter and shape are determined by the machine tooling used to produce them - a die plus an upper and a lower punch are required. This is called a station of tooling. Tablet compression tooling is in intimate contact with the tablets during compression. Smoother tablet production can be achieved by using robust tooling. Selection of tooling material is based on the type of product and past experiences. Different surface treatments can be used to increase tooling life and productivity. Some special design aspects like tapered die bore and Bakelite relief are used to reduce the tablet defects. Proper maintenance of tooling helps in achieving tablet quality standards with respect to the regulatory requirements.

1.6 Important Terminology 1.6.1 Punch

Punch head is the end part of the punch that moves in the cam tract. Flat surface of punch head that is contacted by compression rollers at the time of compression is known as head flat. Angle of the punch head that contact first to the compression roller is known as Outside head angle, where as angle that contacts lift up cam (upper punch) and pull down cam (lower punch) is known as Inside head angle. Neck is the part of punch between head and barrel. Tip length is the vertical distance between the end of punch tip and tip to stem radius. Rounded face of tablet is formed by the curved part of punch tip face known as punch cup. Land is the distance between the edges of punch cup and punch tip. Key is used to align the punch in unidirectional vertical way in unusual (other than round) shapes of tablets.

1.6.2 Die

Die Outer Diameter is the distance between the two vertical edges of the die. Distance between upper and lower end of the die is known as die height. Die bore is the hollow cylindrical part of the die in which tablet is formed. Chamfer, the end part of the die bore having slightly higher diameter which guides the punch into the die bore. To keep the die in properly aligned position in die pocket die locking screw is used which locks the die groove.



Figure 4: Tooling terminology

1.7 Tooling Standards and Types of Tooling

The rotary tablet press using the basic "B" and "D" type tool configuration was devel Developed in late 1800's by Frank J. Stokes. These configurations are accepted worldwide with slight modifications. There are mainly two standards for tooling- American standard [TSM standard which was previously known as industrial pharmaceutical technology standard (IPT standard)] and European standard [Euro norm standard]. International organization for standardization (ISO) has also developed ISO 18084.2005(E) standard for punches and dies.

Tuble 1.7. Types of tooling [20]							
Tool parameter	BB(inch)	B(inch)	D(inch)				
Upper punch length	5 1/4	5 ¼	5 ¼				
Barrel	3⁄4	3⁄4	1				
Head	1	1	1 1⁄4				
Die outer diameter (1)	0.945	0.945	1 1/2				
(2)	1 3/16	1 3/16	1 3/16				
Lower punch length	5 1/4	3 9/16	5 ¼				
Depth of fill	11/16	11/16	13/16				

 Table 1.7: Types of tooling [20]

1.7.1 Causes of Tooling Problems

Sometimes tablet compression tooling is associated with certain problems. Causes for these problems can be divided into formulation problems and mechanical problems. Formulation problems includes moisture content, abrasiveness of materials, humidity etc. uneven wear of punches, corrosion of punch faces, improper polishing and buffing, higher compression forces etc. can be described under mechanical problems. The wear and corrosion experienced during normal tableting operations due to formulation problems may degrade and roughen the tooling surface and the tableting tooling does not perform better and longer. Mechanical problems like uneven wear of punches may affect the dose uniformity of the tablets. Corrosive and improperly polished punch cup faces may cause the failure of the tablets to meet the quality standards.

2. CONCLUSION

Among the different routes of drug administration, oral route is mostly preferred. About 90% of drugs are administered orally for systemic effect. Various kinds of solid dosage forms like tablet, capsules, pills, syrups etc are administered through oral route of drug administration. In orally administered dosage forms, tablet represents the preferred choice of class of product. The tablet is convenient, in terms of self medication, ease of administration, compactness, accurate dose, avoidance pain, versatility and most importantly patient compliance.

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