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Research Article

Comparative Evaluation of Tablets and Liquid-Solid Tablets: An Overview

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ABSTRACT

Oral route of administration is the convenient and safest route of administration. And of all the available dosage forms solid dosage forms like tablets are most widely used due to their stability and patient acceptability and preferred over other dosage forms as they are easy to formulate. These solid dosage forms contain medicaments with/without excipients and compressed as tablets by using machines known as Presses. Now-A-days tablets are prepared by using novel technique known as Liquid-solid compact which is a new and promising addition towards novel to enhance solubility and dissolution of poorly soluble drugs to increase bioavailability. This article's aim is to review the Formulation, Characterization, types, defects and evaluations of tablets and formulation parts and preparation of liquid-solid compacts.

Keywords: Liquid solid compacts; Poor water soluble drugs; Dosage

INTRODUCTION

Tablets which are prepared from dry powers are defined as solid pharmaceutical dosage forms containing drug substances with or without suitable diluents and manufactured either by Wet granulation, Dry granulation or direct compression method [1-5]. Tablets found in market are in different shapes, strengths and combinations of APIs. Tablets are solid, flat or biconvex dishes and unit dosage forms prepared by compressing drug/mixture of drugs with/without diluents. Majority of dossiers are available as tablets, which can be easily swallowed and have immediate or sustained release action [6-12].

At the same time few APIs which are in development are poorly soluble and require alternate formulations to achieve oral bioavailability. Dissolution stands the rate limiting factor for few pharmaceutical formulations; hence the solubility of poorly soluble drugs is increased by micronisation, complexation with beta-cyclodextrins etc. One of the best choices is to develop lipid based formulations but being liquids, these are converted into solid forms *via* adsorption onto solid porous carriers. This can be termed as liquid-solid tablet formulation. This is the technique in which liquid drug developed by changing liquid oleophilic drug or drug solution into a dry, non-adherent, free flowing and readily compressible mixture by mixing it with selected materials. The liquid is either liquid drug, drug suspension or drug solution which is incorporated into porous carrier material. The water miscible organic solvent system with high-boiling point like propylene glycol, liquid polyethelene glycols or glycerine are best examples of liquid vehicles. Once the carrier is saturated with liquid, a liquid layer is formed on particle surface and adsorbed by fine coating particles. The sorbents used for loading lipid formulations are selected through screening studies [13-18].

LITERATURE REVIEW

Comparison of advantages of liquid-solid tablets over tablets

Tablets are light, compact and are available at low cost. These are more stable towards microbial and chemical reactions compared to other dosage forms. They have greater dose precision. Bitter taste can be masked by coatings/addition of taste masking agents. Whereas Liquid-Solid tablets also have similar production to conventional tablets, these are economical than soft gelatine capsules and industrial production is possible. They have enhanced bioavailability compared to conventional tablets. Moreover drug can be molecularly dispersed within formulation and bigger drug extent is exposed to dissolution medium. It omits the approaches like micronisation, nanonisation etc [19].

Disadvantages of tablets

- Difficult to swallow in case of children and unconscious patients
- Drugs with objectionable or bitter taste demand a special masking of the same.
- Some drugs pose challenges during compression owing to their low compressibility or poor binding ability to hold the materials in-tact.

Ingredients

In a tablet formulation, in addition to the drug, other excipients

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Received: August 26, 2021; **Accepted:** September 10, 2021; **Published:** September 17, 2021

Citation: Baddam SR, Manthani A (2021) Comparative Evaluation of Tablets and Liquid-Solid Tablets: An Overview. Drug Des. 10:192.

like diluents, binders, lubricants and so on are also employed. This article discusses about the formulation aspects of Tablets and Liquid-Solid Tablets. The role of the excipients is to modify the drug release characteristics, enhance solubility and bio-availability, increase patient compliance and have impact on tablet weight or volume (Table 1).

Diluents

In a tablet formulation diluents are used to produce bulk known as bulking agents. MCC (Avicel) is most commonly found in formulations. And direct compressible diluents are calcium phosphate, Spray dried Lactose and Anhydrous Lactose. Pre-blended vehicles where API directly added to dry powder and compressed as is Sta-RX 1500 (Self Binding and Disintegrating). There is an interesting diluent known as EMDEX which is a hydrolysed starch used when greater strength tablets are desirable.

Binders

Although diluents hold the tablet powder together binders often used. Most of the binder solutions are prepared by using water except in case of "Tragacanth" which acts as better binder in dry form than moist. Though starch act as diluents in large volumes it also act as binder after hydrating with water (2% w/w).

Lubricants: In tablets lubricants are used to reduce the friction between tablet and press walls. These are generally found in <1%w/w in a formulation.

Glidants: These are used to enhance the flow characters. Corn starch in concentration of 5%-10% w/w act as glidant.

Anti-adherents: These are added to prevent tablets from sticking to walls. E.g. Talcum powder 5% w/w, magnesium carbonate etc.

Disintegrants: These are used in tablet formulations to break the tablet, i.e., when comes in contact with water disintegrant swells and breaks apart. The concentration of disintegrate in tablet formulation is 0.5%-5%.

Absorbents: These are used in case if substance has high affinity for water.

Colouring agents: These are used to distinguish one product from another and also provide visual homogeneity. In wet granulation dye dissolved in binder.

Flavouring oils: These are needed for chewable tablets with the concentration of 0.5% or less (Table 2).

Preparation of tablets

The tablets which are manufactured should meet the requirements of GMP (Good Manufacturing Practices). The following measures which have to be taken during the production of the tablets are:

- Ensure that active ingredient has good solid-solid properties like particle size distribution and polymorphic form and all excipients should ensure homogeneity.
- Tablet should posses' suitable mechanical strength.
- In addition when scored tablets are manufactured the following measures should be taken that ensure the effectiveness with respect to uniformity of subdivided parts, so that patient can receive intended dose.

In general tablets are manufactured by using compression technique with the help of machine known as presses. The main components of presses are hopper, guiding scrapper, dies, punches and cams. When material places in hopper with help of feeder it is

Table 1: Formulation of tablets.

Formulation of tablets		
S.no.	Excipients	Examples
1	Diluents	Carboxymethylcellulose, starch, pregelatinised starch, sorbitol, mannitol, MCC, Calcium phosphate etc
2	Binders	Acacia, Alginic acid, Carboxymethyl cellulose, cellulose, starch, gelatine, liquid glucose, maltodextrin, povidone, zein, HPMC etc
3	Lubricants	Calcium stearate, Glyceryl palmitostearate, magnesium oxide, polaxamer, PVA, SLS, SSS, Stearic acid, Zinc stearate etc
4	Glidants	Cellulose, Starch, Talc, Tribasic -calcium phosphate etc
5	Anti-adherents	Corn starch, Talc, Metallic stearate etc
6	Disintegrants	Alginicacid, Carboxymethylcellulose,Celuylose colloidal silicon dioxide, Cross -carmellose sodium, Cross- povidone, Povidone, Potassium Polacrilin etc
7	Colouring agents	FDand C or DandC dyes or lake pigments
8	Flavouring agents	Ethyl vanillin, Menthol etc
9	Absorbents	Kaolin, Magnesium aluminium Silicate, Tri-calciumPhospate,

Table 2: Formulation parts of liquid-solid tablets.

Formulation parts of liquid-solid tablets		
S. No.	Excipients	Examples
1	Carrier material – These are massive, preferably porous particles possessing a comfortable absorption properly that contributes to liquid absorption.	Various grades of Polyose, Starch22, Lactose 25, Sorbitol 26 etc
2	Coating material – These are very fine (10 nm -5000 nm in diameter) unit flow enhancing, extremely surface assimilation coating particles contribute in covering wet carrier particles and displaying a dry looking powder.	Silica of various grades like Cab-O-SilM5, Aerosil 200, Syloid 244 FP etc
3	Non-Volatile solvents – These are inert, high boiling purpose water miscible and not highly viscous organic solvent systems.	Glycerin, polysorbate, N,N-dimethylacetamide, Fixed oils etc
4	Disintegrates – These are used to break the tablet into pieces when comes in contact with water.	Atomic number 11 starchglycolate
5	Lubricants – Used to reduce the friction between tablet and press walls.	Magnesium stearate

distributed into die cavity. The upper punch descends with force guided by cams to compress material into tablets. With the help of lower punch the tablet which is formed release from die cavity. The size of the die is determined by the position of lower punch. Punches influence the shape of tablets as well. Some tablets are shaped like capsules for easy swallowing known as Caplets. The three methods of preparation of tablets are:

- **Wet granulation method:** This is the most commonly used method and involves the various steps like dispensing of ingredients, Blending in which API, diluents and disintegrant are mixed together and passed through sieve (shifting). Then binder solution is added to initial mixture and amount taking should be sufficient in order to avoid over-wetting of tablets. Tray drying is common method of drying the tablet granules and now this method is replaced by Fluid-Bed dryer as novel approach. After drying they pass through screen usually 60-100 mesh nylon cloth used. After that Lubricants are added and blended properly and compressed as tablets.
- **Dry granulation method:** This method is preferred when ingredients are highly sensitive to moisture or cannot withstand to elevated temperatures during drying. Slugging may be used for granulation. In this method API, Diluents and Lubricant are blended together to form slug and this is passed through mesh or mill. Remaining Lubricant is added to granulation, blended properly and compressed to form tablets.
- **Direct compression method:** This is the method in which drug constitutes major portion of tablet total weight. Tablets containing 25% or less of drug substance can be formulated using suitable diluents which acts as vehicle or carrier. Tablets prepared by direct compression are subjected to compression may be single/multiple stations.

General properties of tablets

- The tablet must be strong and hard to withstand mechanical shock during dispensing, manufacturing, packaging and shipping.
- Tablet should have uniformity in weight and drug content.
- Tablets should have elegant product identity and free from defects.
- They must be physically and chemically stable during manufacturing, storage and use.
- The tablets must produce sufficient bioavailability i.e., it must be able to release its contents in predictable and reproducible manner.

Preparation of liquid-solid tablets

For these tablets firstly take a calculated amount of weighed pure liquid drug or drug dissolved in suitable amount of solvent. For attaining good flow properties Trial and Error methods are used by changing the ratio of carrier: coating material from 50:1 to 5:1.

The liquid material is poured onto the carrier material and is absorbed into carrier internally and externally. And then add the disintegrates. Finally coating material is added for dry looking and for achieving good compression properties. Here both absorption and adsorption take place as the material is going internally and forming layer externally. Excipients which are used in these formulation posses' fine and high adsorption properties such as various types of Amorphous Silicon dioxide (Silica).

Before compression various ingredients such as Lubricants, disintegrates, polymers and binders may be mixed with finished liquid-sold systems to produce Liquid-Solid compacts in form of Tablets or Capsules.

$$\textit{Drug or non} - \textit{volatile solvent} \xrightarrow{\textit{add}\quad \textit{carrier/coated material}} \textit{Mixandadd} \downarrow$$

$$\textit{Compressed to tablets} \leftarrow \textit{add dia}\,\text{int}\,\textit{egrates} \leftarrow \textit{powder form}$$

Method of preparation of Liquid-Solid tablets

Types of tablets

Uncoated tablets: contains active and excipients which are compressed together without any coat/cover.

Coated tablets: are those which have additional coating on tablet surface. These coatings include Gums, sugar, plasticizer and waxes.

Sugar coated tablets: These are compressed tablets coated with concentrated sugar solution to improve patient compliance, increase appeal, mask objectionable taste or odor and increase stability. But the problem with this coating is high cost of process, validation and shipping.

Film-coated tablets: These are conventional tablets which are coated with thin layer of polymers like HPMC, HPC or mixture of polymers like Eudragit E100 (forms skin like film). The characteristic are similar to sugar coating but it has added advantages of more durability, less bulky and less time consuming to apply. By this composition water is designed to break and explore core tablet at desired locations in GIT example Diclofenac potassium USP100 mg.

Enteric-coated tablets: This type of coating is used for delayed release properties. The coating polymers are Cellulose acetate phthalates/Cellulose acetate butyrates, HPMC succinate and Methacrylate acid copolymers. These coatings resist the gastric fluid but disintegrate the tablet and allow drug dissolution and absorbs in the intestine. The Enteric coatings are primarily employed when drug is inactivated or destroyed by Gastric fluid E.g.: Erythromycin or when drug causes irritation to gastric mucosa Ex NSAIDs.

Dispersible tablets: These are film coated/uncoated tablets which undergoes uniform dispersion when suspended in water.

Effervescent tablets: are uncoated tablets when placed in organic acid to dissolve producing CO_2. This carbon dioxide helps in disintegration of tablets and produces suspension of powdered material which is readily absorbed.

Chewable tablets: Chewable tablets are big sized and cannot be swallowed and hence these are chewed within buccal cavity. These tablets are especially for conventional or ant-acid formulations. E.g. Gestid tasty chewable ant-acid.

Buccal or sublingual tablets: These are small, flat, oval tablets intended to be dissolved in buccal pouch or beneath the tongue for absorption through oral mucosa to produce a systemic effect. These tablets are employed to achieve rapid absorption into systemic circulation. E.g Glyceryl trinitrate sublingual tablets.

Tablet problems or tablet defects

Defects related to tableting process:

1. Capping: The term used when upper and lower segment of tablet separates horizontally.

Reason: Air entrapment during compression.

Causes and remedies**:** Large amount of fines or too dried materials causes capping so remove fines through 200 size mesh or moist granules or add hygroscopic materials like sorbitol, PEG400 etc.

2. Lamination: It is the separation of a tablet into 2 or 3 layers horizontally.

Reason: Air entrapment during compression

Causes and remedies: Oil or waxy materials in granules, too much of hydrophobic materials causes lamination so add adsorbents or absorbents and add less lubricants.

3. Cracking: Small, fine cracks are observed on upper and lower surface of tablets. Reason – Rapid expansion of tablets

Causes and remedies: Large size granules too dry granulation or granulation too cold causes cracking so reduce the granule size most them and compress at room temperature.

Defects of tablets related to excipients:

1. **Chipping:** It is defined as the breaking of tablet edges while tablet leaves the press or during handling and coating operations.

   Reason: More binder in formulation

   Causes and Remedies: Too much of binding leads to chipping or sticking on punch faces causes chipping so optimize the binding or use dry binders and dry granules properly.

2. **Sticking/Filming:** It refers to adhering of the material to die wall whereas filming is a slow form of sticking due to excess moisture in granulation.

   Reasons: Improper drying and improper lubrication of granules

   Causes and remedies: Improper drying, improper lubrication, too much binder or oily/waxy materials causes sticking so dry the granules properly and add sufficient lubricants.

3. **Picking:** It is defined as when small amount of material from a tablet is sticked to and removed off from tablet surface by punch face.

   Reasons: When punch face having engraving or embossing letters.

   Causes and remedies: Low melting point medicament in high concentrations, too warm granules during drying/too much amount of binder leads to picking so compress at room, temperature, add high melting point materials or reduce amount of binders.

4. **Mottling:** It is defined as the uneven distribution of colour on the surface of the tablet with light or dark spots standing out in an otherwise uniform surface.

Defects related to machine

Double impression: It involves only those punches which have monogram or other engraving on them.

Causes: Free rotation of punches

Remedies: Use keying in tooling i.e., placing a key alongside of punch, so that it fits the punch prevent punch rotation.

Evaluation of tablets

After the tablet compression, tablets are subjected to various evaluation tests to ensure tablets withstand sufficient mechanical strength.

General appearance

General appearance of a tablet is its identity and general elegance. It is essential for consumer acceptance, for control of Lot-to-lot uniformity, and tablet to tablet uniformity. General appearance involves measurement of size, shape, colour, taste, presence/absence of odor.

Size and shape: Measured by using Micrometer and should controlled within a +/-5 variation of standard.

Organoleptic characters: There should be no mottling on surface of tablet and should have uniform distribution of colour. For visual comparison compare the colour of sample against standard.

Hardness and friability: Tablets must have better strength and hardness to withstand mechanical shocks during manufacturing, packaging and shipping. Hardness is the measure of tablet crushing strength. Whereas friability is determined by using roche friabilator. It consists of plastic chamber which revolves 25 RPM for 4 min. After the tablets are dropped, they are reweighed and the loss of tablet must be 0.5 – 1% is acceptable.

Drug content and release

Weight variation: In this test 20 tablets are weighed individually calculate the average weight. The tablet passes the USP test if no more than 2 tablets are outside the percentage limits and if no tablet differs by more than 2 times percentage limit (Tables 3 and 4).

Content uniformity test: In this method 30 tablets are selected randomly and 10 of these are assayed individually. The tablet passes test if 10 tablets contain NLT 85% and more than 115% of labelled drug content and 10^{th} tablet may contain NLT 75% and more than 125% of labelled drug content. If these conditions not met remaining 20 tablets are assayed and none may fall outside 85-115% range.

Disintegration test: This is the test used to determine the time taken for the tablets to breakdown into pieces in GI tract.

Apparatus: It has a mesh aperture of 2 mm (10#),

Cycles: 28 to 32 cycles/min,

Dissolution test: This test is used to measure the extent and rate of solution formation from dosage forms such as tablets, capsules etc. The dissolution of drug is important for its bioavailability and therapeutic effectiveness. Apparatus of dissolution according to USP are

Type 1-Basket type

Type 2-Paddle type

Table 3: Determine the time taken for the tablets to breakdown into pieces in GI tract.

Limit	IP/BP	USP
10%	80 mg or less	130 mg or less
7.50%	More than 80 mg or less than 250 mg	130 mg to 324
5%	250 mg or more	More than 324

Table 4: Determination of time taken for the tablets to breakdown into pieces in GI tract.

Determination of time taken for the tablets to breakdown into pieces in GI tract	
Uncoated tablet	NMT 15 min, in water
Coated tablet	NMT 30 min in water for film coated tablet and NMT 60 min other than film coated tablets.
Enteric coated tablet	Intact for 1 hr in 0.1 N Hcl and disintegrate within 2 hr in mixed 6.8 phosphate buffer. According to USP 1 hr in simulated gastric fluid and 1 hr in simulated intestinal fluid.
Dispersible/soluble tablet	Within 3 min in water at 25°C +/-1°C (IP) and 15°C-25°C (BP).
Orodispersible tablet	Within 1 min
Effervescent tablet	5 min in 250 ml of water at 20°C-30°C (IP) and 5 min in 200 ml of water at 15°C-25°C
Buccal and Sublingual tablet	Not applicable but dissolve within 15-30 min
Distance from bottom and top -50 mm to 60 mm, Temp of water -37°C +/-2°C. If 1 or 2 tablets fail, repeat for 12 tablets.	

Type 3-Reciprocating cylinder

Type 4-Flow through cell

Type 5-Paddle over disc

Type 6-Rotating cylinder

Type 7-Reciprocating disc

According to IP Type 1 is the paddle and Type 2 is the basket type apparatus.

CONCLUSION

All the solid dosage forms Tablets are more popular as they are acceptable by patients as well as provide self-administration. In case of poorly soluble drugs tablets can be prepared by using novel technique known as Liquid-Solid compaction. These liquid-solid compacts are helpful to overcome the low bioavailability of drugs. These liquid-solid tablets contain liquid lipid drug which is absorbed or adsorbed onto carrier and mixed with other excipients and compressed as tablets. During manufacturing of tablets many problems arise during in-process and finished products and these are arrested by using proper preventive methods. Hence Quality Control tests on finished products are required.

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