ADVANTAGES OF IMMEDIATE RELEASE TABLETS OVER THE OTHER TABLET FORMS.

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ABSTRACT

In the present time most common and widely useful route of administration of maximum drug is oral route; in which tablet form is widely used dosage form over the other dosage form because of self-administration and ease in formulation. Mostly drug are available with BCS class I, II & IV, so there should be the first main target to develop a formulation with increasing solubility & permeability. Mostly Drugs have half-life of is about 1.5 to 3 days. So there is another essential need to devolvement a formulation of such poorly water soluble drug with different approaches to enhance bioavailability of the drug. There is also need of rapid dissolution and absorption of drug, which may produce rapid onset of action. Immediate release tablets fulfill these all requirements over the other dosage forms. But after the formulation of product, improper drug release is another problem & improper distribution of drug in blend power during granulation, is the second major problem. Different techniques such as direct compression, dry granulation and wet granulation can be used for formulation of tablets. Proper amount of diluents, disintegrating agents & lubricants in immediate release tablet preparation, become important step to achieve desired bioavailability within desired time. Mostly Pharmaceutical products are available for oral delivery and also available for the prescription and over-the-counter markets, which are the immediate release dosage forms, these dosage forms are only for immediate release of the drug for rapid absorption & rapid onset of action.

KEYWORDS: Immediate release, solubility, dissolution, disintegration agents.

1. INTRODUCTION

Oral route is very common and easy route of administration of drug is oral route because of its systemic effect, patient compliance and cheaper to manufacture. Tablets provide high
precision dosing. Tablet form is the most widely used dosage form cause of self-administration and easy to produce.\textsuperscript{[1]}

It is a solid dosage form each containing some unit dose- one & more medicament/s. Tablet dosage forms are solid, flat or biconvex discs prepared by compressing of drug or combination of drugs with the use of suitable excipients. Tablets may be swallowed whole or being chewed. Some tablets are used with dissolving or disperse in water before the administration. But some tablets are put in oral cavity, where the active ingredient is liberated at a predetermined rate. Implants may also be presented in form of tablet. Tablet may vary in shape and differ greatly in size, weight & others, depends on the amount of drug substance and the intended mode of administration.\textsuperscript{[2]}

The term “immediate release” pharmaceutical formulation includes any formulation in which the rate of release of drug from the formulation and/or the absorption of drug, is neither appreciably, nor intentionally, retarded by galenic manipulations. In the present case, immediate release may be provided for by way of an appropriate pharmaceutically acceptable diluents or carrier, which diluents or carrier does not prolong, to an appreciable extent, the rate of drug release and/or absorption. Thus, the term excludes formulations which are adapted to provide for “modified”, “controlled”, “sustained”, “prolonged”, “extended” or “delayed” release of drug.\textsuperscript{[25]}

\textbf{1.1. Types of Tablets}\textsuperscript{[2]}

\textit{1.1.1. Compressed tablets}

These tablets are formed by compression and contain no special coating. They made from powdered, crystalline, or granular material, alone or in combination with binder, disintegrates, controlled release polymer, lubricant, and diluents and in many cases colorant.

\textit{1.1.2. Sugar-coated tablets}

Sugar-coated tablets are such type of compressed tablets which containing a sugar coating. Such coating may be colour and beneficial to covering up drug substances having unpleasant taste or odour and in protecting material sensitive to oxidation.

\textit{1.1.3. Film coated tablets}

These are compressed tablets that covered with thin layer of film of water soluble material. A number of materials with film forming properties are used.
1.1.4. Enteric coated tablets
These are compressed tablet which coated with substance that can resist in gastric fluid but disintegrate in intestine. Enteric coating can be use for tablets those containing medicinal substances that are remains inactivated & destroyed in stomach, for those that irritates the mucosa, or as a means of delayed release of medication.

1.1.5. Multiple compressed tablets
These are compressed tablets made by more than one compression cycle; Layered tablets, Pressed -coated tablets.

1.1.6. Controlled released tablets
Compressed tablet can be formulated to release the drug slowly over prolonged period of time. Hence this dosage form referred also as sustained released & prolonged-release dosage form.

1.1.7. Tablets for Solution
Compressed tablets to be used for preparing solution or imparting given characteristic to solution must be labelled to indicate that they are not to be swallowed.

1.1.8. Effervescent tablets
In addition to drug substances these tablets contains sodium bicarbonate and organic acid such as tartaric acid or citric acid. In presence of water these additives react, liberating carbon dioxide that act as disintegrator and produces effervescence.

1.1.9. Compressed suppositories or insert
Vaginal suppositories are prepared by compression such as metronidazole. Tablet for this use usually contain lactose as the diluent.

1.1.10. Buccal or sublingual tablets
These are small, flat, oval tablets. Tablets intended for buccal administration by inserting into buccal pouch, may dissolve or erode slowly therefore they are formulated and compressed with sufficient pressure to give a hard tablet.

1.1.11. Molded tablet or tablet triturates
Tablet triturates are made from moist material, using triturate mold that gives the shape of cut section of cylinder. Such tablets must be completely and rapidly soluble.
1.1.12. Dispensing tablets
These tablets provide the convenient quantity of potent drug that can be incorporated readily into powders and liquid, thus circumventing the necessity to weight small quantities.

1.1.13. Hypodermics tablets
Hypodermic tablets are soft, readily soluble and originally were use for the preparation of solution to be injected.

1.2. Immediate Release Tablets
Immediate release tablets are those which disintegrate rapidly and get dissolved to release the medicaments. Immediate release may be provided for by way of an appropriate pharmaceutically acceptable diluent or carrier, which diluent or carrier does not prolong, to an appreciable extent, the rate of drug release and/or absorption.[1]

Immediate release tablet are also called as Fast – dissolving tablets, Melt-in mouth tablets or dispersible tablets, Rapimelts, Porous tablets, Quick dissolving etc. Fast dissolving tablets are those when put on tongue disintegrate instanteously releasing the drug which dissolves or disperses in the saliva. The Faster the drug into solution, quicker the absorption and onset of clinical effect some drugs are absorbed are absorbed form the mouth pharynx and esophagus as the saliva passes down into the stomach In Such cases bioavailability of drug is significantly greater than those observed form conventional tablets dosage form.[2][3]

The release of drug from the conventional tablet dosage form and its absorption from the GIT depends upon two main processes: first- the disintegration of tablet into granules and second- dissolution of these granules through the GIT into the blood. Disintegration is the rate limiting step in case of highly soluble drugs whereas dissolution is the rate limiting step in case of drugs with low solubility.
The release of drug from an immediate release dosage form can be achieved by placing the drug in a layer or coating that is sufficiently thin to allow fast penetration by gastrointestinal fluid which then leaches the drug at a rapid rate. Incorporating the drug in a mixture that includes a supporting binder or other inert material that dissolves readily in gastrointestinal fluid, releasing the drug as the material dissolves. Using a supporting binder or other inert material that rapidly disintegrates into fine particles, upon contact with gastrointestinal fluid, with both the binder particles and the drug quickly dispersing into the fluid. Conventional dosage forms can be considered to release their active ingredients into an absorption pool immediately. The absorption pool represents a solution of the drug at the site of absorption, and the terms Kr (drug release rate constant), Ka (drug absorption rate constant) and Ke (elimination rate constant) are first-order rate constants for drug release, absorption and overall elimination, respectively. Immediate release from a conventional dosage form implies that kr >> ka or alternatively, that absorption of drug across a biological membrane, such as the intestinal epithelium, is the rate-limiting step in the delivery of drug to its target area.

Disintegrating agents are substances routinely included in tablet formulations and in some hard shell capsule formulations to promote moisture penetration and dispersion of the matrix of the dosage form in dissolution fluids. Superdisintegrants improve disintegrant efficiency resulting in decreased use levels when compared to traditional disintegrants.

Traditionally, starch has been the disintegrant of choice in tablet formulation, and it is still widely used. For instance, starch generally has to be present at levels greater than 5% to adversely affect compatibility, especially in direct compression. Drug release from a solid
dosage form can be enhanced by addition of suitable disintegrants. Superdisintegrants are the agents added to tablet and some encapsulated formulations to promote the breakup of the tablet and capsule “slugs” into smaller fragments in an aqueous environment thereby increasing the available surface area and promoting a more rapid release of the drug substance. [2] [3] [24]

1.2.1 Criteria of immediate release dosage form [4, 5]

- Not require water to swallow, but it should dissolve or disintegrate in the mouth in matter of seconds.
- Ease of administration to patients who refuse to swallow a tablet such as pediatric and geriatric patients and psychiatric patients.
- Convenience of administration and accurate dosing as compared to liquids.
- Be manufactured using conventional processing and packaging equipment at low cost.
- Rapid dissolution and absorption of drug, which may produce rapid onset of action.
- In the case of solid dosage it should dissolve or disintegrate in the stomach within a short period. In the case of liquid dosage form it should be compatible with taste masking.
- Be portable without fragility concern.
- Have a pleasing mouth feel.
- It should not leave minimal or no residue in the mouth after oral administration.
- Exhibit low sensitivity to environmental condition as humidity and temperature.

1.2.2 Need of immediate release tablets [6]

- Patient factors
  Orally disintegrating dosage forms are particularly suitable for patients (particularly pediatric and geriatric patients) who are not able to swallow traditional and capsules with an 8 – oz glass of water.

- Effectiveness factor
  Increased bioavailability and faster on set of action are major claim of these formulations. Dispersion in saliva in oral cavity cause pregastric absorption form some formulations in the those cases where drug dissolves quickly. Buccal pharyngeal and gastric regions are absorption for many drugs. Any pregastric absorption avoids first pass metabolism and can be a great advantage in drugs that undergo a great deal of hepatic metabolism.
Manufacturing factors
Developing new drugs delivery technologies and utilizing them in product development is critical for pharmaceutical industries to survive, regardless of their size. As a drug nears the end of its patent life, it is common for pharmaceutical manufacturers to develop given drug entity in a new and improved dosage form.

1.2.3. Advantages of immediate release tablets

- Accurate Dosing
Being unit solid dosage Forms, Provide of accurate dosing easy portability and manufacturing, good physical and chemical stability and an ideal alternative for pediatric and geriatric patients.

- Enhanced bioavailability
Bioavailability of drug is enhanced due to absorption from mouth pharynx and esophagus.

- Rapid action
Fast onset of therapeutic action as tablet gets disintegrated rapidly along with quick dissolution and absorption in oral cavity.

- Patient compliance
No need of water to swallow the dosage form. Hence it is convenient for patients who are travelling and do not have immediate access to water.

- Ease of Administration
Convenient to administer specially for geriatric pediatric mentally for patients who are travelling and do not have immediate access to water.

- Obstruction Free
No Risk of suffocation in airways due to physical obstruction when swallowed thus providing improved safety and compliance.

- Enhanced palatability
Good mouth feels, especially for pediatric patients as taste masking technique is used to avoid avoiding the taste of drug.
Simple packaging
No specific packaging required. It can be packaged in push through blisters.

- **Business Avenue**
  Provide new business opportunities in the form of product differentiation, line extension uniqueness and life cycle management.

- **Cost Effective**
  Conventional processing and packaging equipment allow the manufacturing of tablets at low cost.

### 1.2.4. Disadvantages of immediate release tablets

- Single dosing of a conventional dosage form cannot maintain drug blood levels within the therapeutic range for an extended period of time.
- Because of the inevitable fluctuation of steady state blood levels, a patient may be overmedicated or under medicated for period of time if the values of $C_{\text{max}}$ and $C_{\text{min}}$ rise or fall, respectively, beyond the therapeutic range of the drug.
- Lack of patient compliance in case of dosage regimens requiring frequent dosing may lead to therapeutic failure / inefficiency.
- Provided the dose size and frequency of administration are constant, repetitive administration of conventional doses forms at a constant interval can achieve therapeutic “steady state” blood levels. But this approach also has a number of potential limitations.
- The blood level of drug fluctuates over successive dosing intervals, even when the so called “steady state” condition is achieved.

### 1.2.5. Potential candidate of immediate release oral dosage form

- Analgesics and Anti-inflammatory agents: aloxiprin, benorylate, diflunisal, etodolac, fenbufen, fenoprofen calcim, ibuprofen, indomethacin, ketoprofen, meclofenamic acid & mefenamic acid.
- Anthelmintics: albendazole, bephenium, hydroxynaphthoate, cambendazole, dichlorophen, ivermectin & mebendazole.
- Anti-Arrhythmic agents: amiodarone HCl, disopyramide, flecainide acetate & quinidine sulphate.
- Anti-bacterial agents: benethamine penicillin, cinoxacin & ciprofloxacin.
- Anti-fungal agents: amphotericin, butoconazolnitrte, clotrimazole, econazolnitrte & fluconazole.
- Anti-gout agents: allopurinol, probenecid & sulphipyrazone.
- CVS agents: amlodipine, carvedilol, benidipine, darodipine, dilitazem HCl, diazoxide, felodipine, digoxin & guanabenz acetate.

1.3. Technique used for the preparation of immediate release tablets

Conventional Techniques

Conventional technique used in the preparation of immediate release tablets

- Tablet molding technique
- Direct compression technique
- Granulation technique
- Mass extrusion technique

Several Technologies are available to manufacture immediate release tablets. The most common preparation methods are moulding, lyophilisation or freeze drying, direct compression, spray drying and sublimation.[11][20][21]

1.3.1. Tablet molding[7]

In this technology, water-soluble ingredients are used so that tablet disintegrate and dissolve rapidly. The powder blend is moistened with a hydroy alcoholic solvent and is molded in to tablet using compression pressure lower than used in conventional tablets compression. The solvent is then removed by air-drying. Molded tablets have a porous structure that enhances dissolution. Two problems commonly encountered are mechanical strength and poor taste masking characteristics. Using binding agents such as sucrose, acacia or poly vinyl pyrrolidone can increase the mechanical strength of the tablet. To overcome poor taste masking characteristic Van Scoik incorporated drug containing discrete particles, which were formed by spray congealing a molten mixture of hydrogenated cottonseed oil, sodium bicarbonate, lecithin, polyethylene glycol and active ingredient into a lactose based tablet triturate form.

1.3.2. Direct compression method[8]

In this method, tablets are compressed directly from the mixture of the drug and excipients without any preliminary treatment. The mixture to be compressed must have adequate flow properties and cohere under pressure thus making pretreatment as wet granulation
unnecessary. Few drugs can be directly compressed into tablets of acceptable quality. A type of disintegrant and its proportion are of prime importance. The other factors to be considered are particle size distribution, contact angle, pore size distribution, tablet hardness and water absorption capacity. All these factors determine the disintegration. The disintegrant addition technology is cost effective and easy to implement at industrial level.

1.3.3. Dry granulation
In dry granulation process the powder mixture is compressed without the use of heat and solvent. The two basic procedures are to form a compact of material by compression and then to mill the compact to obtain granules. Two methods are used for dry granulation. [9] [22]

a. Slugging process[22]
Granulation by slugging is the process of compressing dry powder of tablet formulation with tablet press having die cavity large enough in diameter to fill quickly. The accuracy or condition of slug is not too important. Only sufficient pressure to compact the powder into uniform slugs should be used. Once slugs are produced they are reduced to appropriate granule size for final compression by screening and milling.

Figure 1.2: Slugging Process.
b. Roller compaction

The compaction of powder by means of pressure roll can also be accomplished by a machine called chilsonator. Unlike tablet machine, the chilsonator turns out a compacted mass in a steady continuous flow. The powder is fed down between the rollers from the hopper which contains a spiral auger to feed the powder into the compaction zone. Like slugs, the aggregates are screened or milled for production into granules.

![Figure 1.3: Roller compaction process.](image)

1.3.4. Wet granulation method

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

- The active ingredient and excipients are weighed and mixed.
- 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 corn starch, natural gums such as acacia, and cellulose derivatives such as methyl cellulose, gelatin and povidone.
- Screening the damp mass through a mesh to form pellets or granules.
- Drying the granulation. A conventional tray-dryer or fluid-bed dryer are most commonly used.
- 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.

1.3.5 Mass-Extrusion

This technology involves softening the active blend using the solvent mixture of water-soluble polyethylene glycol and methanol and subsequent expulsion of softened mass through the extruder or syringe to get a cylinder of the product into even segments using heated blade to form tablets. The dried cylinder can also be used to coat granules for bitter drugs and thereby achieve taste masking.[13]

1.4. Problems in tablet manufacturing[14]

An ideal tablet should be free from any visual defect or functional defect. The advancements and innovations in tablet manufacture have not decreased the problems, often encountered in the production, instead have increased the problems, mainly because of the complexities of tablet presses; and/or the greater demands of quality. An industrial pharmacist usually encounters number of problems during manufacturing. Majority of visual defects are due to inadequate fines or inadequate moisture in the granules ready for compression or due to faulty machine setting. Functional defects are due to faulty formulation. Solving many of the
manufacturing problems requires an in-depth knowledge of granulation processing and tablet presses and is acquired only through an exhaustive study and a rich experience.

Following are the defects that are found during tablet manufacturing:

1. Weight variation
2. Capping
3. Lamination / Laminating
4. Cracking
5. Chipping
6. Sticking / Picking
7. Mottling
8. Double impression

Figure 1.4: Tablet Defects.

1.5. Evaluation of immediate release tablet

1.5.1 Evaluation of Blend

The prepared blend is evaluated by following parameters.

a. Angle of repose

Angle of repose was determined by using funnel method. The accurately weighed blend was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of blend. The drug (as solid dispersion) excipients blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation.

\[ \tan \theta = \frac{h}{r} \]
b. Bulk Density (BD)

Weigh accurately 25 g of granules, which was previously passed through #20 sieve and transferred in 100 ml graduated cylinder. Carefully level the powder without compacting and read the unsettled apparent volume (V0). Calculate the apparent bulk density in gm/ml by the following formula.

Bulk density = Weight of powder / Bulk volume

c. Tapped density (TD)

Weigh accurately 25 g of granules, which was previously passed through #20 sieve and transfer in 100 ml graduated cylinder. Then mechanically tap the cylinder containing the sample by raising the cylinder and allowing it to drop under its own weight using mechanically tapped density tester that provides a fixed drop of 14± 2 mm at a nominal rate of 300 drops per minute. Tap the cylinder for 500 times initially and measure the tapped volume (V1) to the nearest graduated units, repeat the tapping an additional 750 times and measure the tapped volume (V2) to the nearest graduated units. If the difference between the two volumes is less than 2% then final the volume (V2). Calculate the tapped density in gm/ml by the following formula.

Tapped density = Weight of powder / Tapped volume

d. Carr’s Index

The Compressibility Index of the powder blend was determined by Carr’s compressibility index. It is a simple test to evaluate the BD and TD of a powder and the rate at which it packed down. The formula for Carr’s Index is as below.

Carr’s Index= [(TD-BD)*100]/ TD

e. Hausner’s Ratio

The Hausner’s ratio is a number that is correlated to the flow ability of a powder or granular

Hausner’s ratio = TD/BD

1.5.2 Evaluation of Tablets

To design tablet dosage form, factors like product quality, quantitative evaluation, chemical, physical and biological properties needs to be evaluated by using following parameters.
a. Weight variation
Drug content of tablet were representing as mean ± SD. Tablet weight variation friability were measured using the USP methods and criteria. Twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight.

Weight, of tablet were representing as mean ± SD.

b. Hardness
Hardness (diametric crushing strength) is a force required to break a tablet across the diameter. The hardness of a tablet is an indication of its strength. The tablet should be stable to mechanical stress during handling and transportation. The degree of hardness varies with the different manufactures and with the different types of tablets. The hardness was tested using Dr. Schleunizer hardness tester. Hardness of tablet was measured by Monsanto hardness tester. Hardness of tablet were representing as mean ± SD.

c. Tablet Thickness
Thickness of tablets was important for uniformity of tablet size. The thickness and diameter of tablet of the tablets was determined by using vernier calipers. Randomly 10 tablets selected were used for determination of thickness and diameter of tablet that expressed in Mean ± SD and unit is mm.

d. Friability
Friability is the loss of weight of tablet in the container due to removal of fine particles from the surface during transportation or handling. Roche friabilator was employed for finding the friability of the tablets.

e. In vitro Disintegration test
The various core tablet formulations prepared by wet granulation method are subjected to disintegration studies using 900ml water (as a disintegrating medium) and the time taken for disintegration is noted. The USP device to test disintegration contains six glass tubes that were 77.5 ± 2.5 mm long, open at the top, and held against 10 screens at the bottom end of the basket rack assembly. One tablet is placed in each tube and the basket rack is poisoned in 1 liter beaker of distilled water at 37± 2 ºC, such that the tablets remain below the surface of
the liquid on their upward movement and descend not closer than 2.5cm from the bottom of the beaker.

**f. In vitro Dissolution test**

In vitro dissolution test was carried out by triplicate method using USP Type II (Paddle type) Apparatus. 900ml of distilled water was used as dissolution medium, and the paddle was rotated at 50rpm for 1 hr at a temperature of 370C. Sampling was done at regular intervals and was replaced by water after each sampling interval. The samples are then analyses spectrophotometrically at 315nm.

**g. Wetting time and water absorption ratio**

A piece of tissue paper folded twice was placed in a small petridish (i.d. = 6.5 cm) containing 6 ml of distilled water, a tablet was put on the paper, and the time required for complete wetting was measured. The wetted tablet was then weighed. Three trials for each batch were performed and standard deviation was also determined. Water absorption ratio, R, was determined using equation.

\[ R = 100 \times \frac{(W_a - W_b)}{W_b} \]

Where,

- \( W_b \) = weight of the tablet before water absorption
- \( W_a \) = weight of the tablet after water absorption

**h. Content Uniformity**

**Procedure**

weight accurately fine powder of one tablet then was added into the 10ml volumetric flask having 6ml diluted ethanol (50%). The prepared solution was sonicated for 30 minutes then volume was making up to 10ml with 50% diluted ethanol, then prepared solution was filtered and injected into the chromatic system and Chromatogram was recorded and measures the responses for the analyte peak. Drug X (mg) in one tablet (mg) for the sample preparations was calculated using the following formula (United States Pharmacopoeia, 2003).

\[
\text{Drug X (mg)} = W_s \times p/100 \times A_t/A_s \times V/500
\]
Where,

\[ A_t = \text{Peak Area of the Drug X in the Sample preparation} \]
\[ A_s = \text{Peak Area of the Drug X in the Standard preparation} \]
\[ W_s = \text{Weight of the Drug X Reference Standard taken in mg} \]
\[ P = \% \text{ Assay of Drug X Reference Standard} \]

**i. Stability studies**

The purpose of stability testing is to provide evidence on how the quality of a drug substance or drug product varies with time under the influence of a variety of environmental factors such as temperature, humidity and light, enabling recommended storage conditions, re-test periods and shelf-lives.


**j. Statistical analysis**

All statistical calculations were performed using Sigma Stat 3.5 demo version software. Data were analyzed using student’s’ test and one way analysis of variance (ANOVA). Differences were considered statistically significant at \( P<0.05 \).

**1.6. General excipients used in immediate release tablets**

**1.6.1. Ideal characteristics of excipients\textsuperscript{[15][23]}**

- They must be non-toxic with no pharmacological activity and acceptable to the regulatory agencies in the countries where the product is to be marketed.
- They must be commercially available in an acceptable grade in countries where the product is to be manufacture.
- Cost effective.
- They must be physiologically inert.
- They must be physically and chemically stable by themselves and in combination with other drugs and tablet components.
- They must be free of any unacceptable microbiological load.
- They must be color compatible, should not change shade of color in the formulation.
- If product is classified as food, the diluents and other excipients must be approved food additives.
They must not have an adverse effect on the bioavailability of the products.

### Table 1.1: Lists of different excipients used in the design of tablets\[^{[15]}\]

<table>
<thead>
<tr>
<th>Excipients</th>
<th>Functions</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diluents</td>
<td>Used as filler designed to make up the required bulk of the tablet.</td>
<td>Lactose, starch, mannitol, sucrose, sorbitol etc.</td>
</tr>
<tr>
<td>Binders and Adhesives</td>
<td>These are used to produce cohesive compact, either in dry or wet form.</td>
<td>Hydroxy propyl methyl cellulose, acacia, starch, cellulose derivative etc.</td>
</tr>
<tr>
<td>Disintegrants</td>
<td>Used to facilitate a breakup of the tablet.</td>
<td>Starch, clays, cellulose, alginate, povidone etc.</td>
</tr>
<tr>
<td>Lubricants</td>
<td>Used to reduce the friction during tablet ejection between the walls of die cavity.</td>
<td>Stearic acid, stearic acid salts, polyethylene glycol, talc, waxes etc.</td>
</tr>
<tr>
<td>Antiadherants</td>
<td>Used to reduce sticking or adhesion of any tablet granules or powder to the faces of punches or die wall.</td>
<td>Talc, polyethylene glycol, hydrogenated castor oil, glycercyl behenate etc.</td>
</tr>
<tr>
<td>Glidants or flow promoters</td>
<td>Used to promote flow of the tablet granules or powder material by reducing friction within particles.</td>
<td>Silica derivatives, talc, corn starch etc.</td>
</tr>
<tr>
<td>Colors, flavors and sweeteners</td>
<td>Used to enhance the Organoleptic properties and acceptability of the product.</td>
<td>FD &amp; C, D&amp;C dyes and lakes, banana, bubble gum, strawberry, vanilla flavors, aspartame, neotame, saccharin, mannitol etc.</td>
</tr>
</tbody>
</table>

**a. Disintegrants\[^{[15]}\]\[^{[21]}\]**

As disintegrants sodium starch glycolate, sodium carboxymethyl cellulose, calcium carboxymethyl cellulose, croscarmellose sodium, Crospovidone, polyvinyl polypyrrrolidone, methyl cellulose, microcrystalline cellulose, powdered cellulose, lower alkyl-substituted hydroxypropyl cellulose, polacrilin potassium, starch, pregelatinized starch, sodium alginate, and mixtures thereof. The amount of disintegrant included in the dosage form will depend on several factors, including the properties of the dispersion, the properties of the porosigen and the properties of the disintegrant selected. Generally, the disintegrant will comprise from 1% w/w to 25% w/w of the dosage form.

**Mechanism of tablet Disintegration**

The tablet breaks to primary particles by one or more of the mechanisms listed below:

1) By capillary action
2) By swelling
3) Because of heat of wetting
4) Due to disintegrating particle/particle repulsive force
5) Due to deformation
6) Due to release of gases
7) By enzymatic action

Table 1.2: Classification of superdisintegrants

<table>
<thead>
<tr>
<th>Sr no.</th>
<th>Structure type</th>
<th>Description</th>
<th>Trade name</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>Modified starches (Sodium starch glycolate)</td>
<td>Sodium carboxy methyl starch, the carboxymethyl groups induced hydrophilicity and cross-linking reduces solubility.</td>
<td>Explotab Primojel</td>
</tr>
<tr>
<td>2.</td>
<td>Modified cellulose (Crosscarmallose NF)</td>
<td>Sodium carboxy methyl cellulose which has been cross-linked to render the material insoluble.</td>
<td>Ac-Di-Sol NymcelSolutab</td>
</tr>
<tr>
<td>3.</td>
<td>Cross-linked polyvinylpyrrolidone (Crosspovidone)</td>
<td>Cross-linked polyvinylpyrrolidone, the high molecular weight and cross-linking render the material insoluble in water.</td>
<td>Crosapovidone Kollidon Polyplasdone</td>
</tr>
</tbody>
</table>

b. Binder

Binder is a material used to bind other materials together. Microcrystalline cellulose (MCC) is commonly used as a filler-binder in direct compression because of its good bonding properties. Other commonly used binders in direct compression include starches and their derivatives, such as pregelatinised and granulated starches.

c. Surfactants

One very useful class of excipients is surfactants, preferably present from 0 to 10 % w/w. Suitable surfactants include fatty acid and alkyl sulfonates; commercial surfactants such as benzalkonium chloride, dioctyl sodium sulfosuccinate, polyoxyethylene sorbitan fatty acid esters, natural surfactants such as sodium taurocholic acid, lecithin, and other phospholipids and mono and diglycerides; and mixtures thereof. Such materials can advantageously be employed to increase the rate of dissolution by, for example, facilitating wetting, or otherwise increase the rate of drug release from the dosage form.

d. pH Modifiers

Inclusion of pH modifiers such as acids, bases, or buffers may also be beneficial in an amount of from 0 to 10 % w/w. Acidic pH modifiers (e.g., acids such as citric acid or succinic acid) retard the dissolution of the pharmaceutical composition when the dispersion polymer is anionic. Alternatively, basic pH modifiers (e.g., sodium acetate or amines) enhance the rate of dissolution of the same types of pharmaceutical composition.
e. Diluents
Examples of other matrix materials, fillers, or diluents include lactose, mannitol, xylitol, dextrose, sucrose, sorbitol, compressible sugar, microcrystalline cellulose (MCC), powdered cellulose, starch, pregelatinized starch, dextrates, dextran, dextrin, dextrose, maltodextrin, calcium carbonate, dibasic calcium phosphate, tribasic calcium phosphate, calcium sulfate, magnesium carbonate, magnesium oxide, poloxamers, polyethylene oxide, hydroxypropyl methyl cellulose (HPMC) and mixtures thereof.

f. Lubricants
Examples of lubricants include calcium stearate, glyceryl monostearate, glyceryl palmitostearate, hydrogenated vegetable oil, light mineral oil, magnesium stearate, mineral oil, polyethylene glycol, sodium benzoate, sodium lauryl sulfate, sodium stearyl fumarate, stearic acid, talc and zinc stearate.

g. Glidants
Examples of glidants include silicon dioxide, talc and cornstarch. A glidant is a substance that is added to a powder to improve its flowability. A glidant will only work at a certain range of concentrations. Above a certain concentration, the glidant will in fact function to inhibit flowability (which means that there's a critical concentration to be used if increasing powder's flowability is intended with respect to the glidant and the powder properties). In tablet manufacture, glidants are usually added just prior to compression.

2. SUMMARY AND CONCLUSION
Oral route of drug administration is perhaps the most appealing route for the delivery of drugs. Among various dosage forms administered orally, the tablet is most preferred dosage forms because of its ease of manufacturing, convenience in administration, accurate dosing, stability compared with oral liquids and because it is more tamper proof than capsule and suspension. The drugs administered by oral route are versatile, flexible in dosage strength, relatively stable, present lesser problem in formulation and packaging and are convenient to manufacturer, store, handle and use. Solid dosage forms provide best protection to drugs against temperature, light, oxygen and stress during transportation. The bioavailability of drug is dependent on in vivo disintegration, dissolution and various physiological factors. In recent years, scientists have focused their attention on the formulation of immediate release (IR) tablets. The task of developing immediate release tablet is accomplished by using a suitable diluents and super-disintegrants. Faster disintegration of the tablet administrated...
orally minimizes absorption time and improves its bioavailability in less time. Bioavailability of the drug is one critical parameter for determining the efficacy of pharmaceutical formulations. The therapeutically effective amount of a medicine in a composition should be made available at the site of action with optimum blood concentrations of the active ingredients reached within the shortest possible time.

There is a need for dosage forms which have all the advantages of a tablet or capsule formulation and the bioavailability and convenience of administration of a suspension. An immediate release tablet is one such dosage form which meets the needs. They are easy to carry and administered to patients accurately and conveniently. Hence immediate release tablet serves the purpose over sustain release and controlled release formulations. Important studies included in the present investigation are the effect of disintegrants, lubricants and binder on performance of the immediate release (IR) tablets. The process parameters selected were the effect of Intragranular disintegrant quantity, Extragranular disintegrant quantity, Loss on drying and effect of hardness and thickness. The effect of selected process parameters on critical properties of IR tablets were studied, like effect of disintegration time, friability, dissolution profile.

Immediate release tablets are those which immediately disintegrate and release the drug as it enters in Gastro-intestinal tract. Immediate release tablet is highly popular and acceptable formulation of oral drug delivery system mainly because of easy administration and better patient compliance. Immediate release tablets are those tablets which are formulated to disintegrate and release drugs immediately in the gastrointestinal tract, without any special rate controlling system such as special coating or other techniques. As many of the drug falls under the category of poorly water soluble or water insoluble drugs, solubility enhancement becomes important step to achieve desired bioavailability within desired time. The fact that the major class of drugs are poorly water soluble which limits their use in oral drug delivery system such as tablets. In such cases dissolution step is rate limiting step and thus there is a need to develop formulation of such poorly soluble drug with different approaches to enhance solubility and oral bioavailability of drug. If the half-life of the any drug is about i.e., 1.5 to 2 days. It has narrow Therapeutic window of drug. There is need of rapid dissolution and absorption of drug, which may produce rapid onset of action.

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.

3. REFERENCES


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