ABSTRACT
Tablet is the most popular among all dosage forms existing today because of its convenience of self administration, compactness and easy manufacturing; however in many cases immediate onset of action is required than conventional therapy. To overcome these drawbacks, immediate release pharmaceutical dosage form has emerged as alternative oral dosage forms. There are novel types of dosage forms that act very quickly after administration. The basic approach used in development tablets is the use of superdisintegrants like Cross linked carboxymethylcellulose (Croscarmellose), Sodium starch glycolate (Primogel, Explotab), Polyvinyl pyrrolidone (Polyplasdone) etc. which provide instantaneous disintegration of tablet after administration. Immediate release liquid dosage forms and parenteral dosage form have also been introduced for treating patients. dosage form can be suspensions with typical dispersion agents like hydroxypropyl methylcellulose, (dioctylsulfosuccinate) etc. The development of immediate release therapy also provides an opportunity for a line extension in the marketplace, A wide range of drugs (e.g., Antidiabetic, neuroleptics, cardiovascular drugs, analgesics, antihistamines and drugs can be considered candidates for this dosage form.

KEYWORDS: immediate release, superdisintegants, compactness.

INTRODUCTION
Oral administration is the most popular route for systemic effects due to its ease of ingestion, pain, avoidance, versatility and most importantly, patient compliance. Also solid oral delivery systems do not require sterile conditions and are therefore, less expensive to manufacture. Patient compliance, high-precision dosing and manufacturing efficiency make tablets the solid dosage form of choice. Excipients and equipments choices will be significantly affected should solid dosage form technologies change in response to the unprecedented shifts in the
drug discovery such as genomics. Injections generally are not favored for use by patients unless facilitated by sophisticated auto injectors. Inhalation is one good alternative system to deliver these drugs, but the increased research into biopharmaceuticals so far has generate predominantly chemical entities with low molecular weights.

The development of enhanced oral protein delivery technology by immediate release tablets which may release the drugs at an enhanced rate are very promising for the delivery of poorly soluble drugs high molecular weight protein and peptide. The oral route remains the perfect route for the administration of therapeutic agents because the low cost of therapy, manufacturing and ease of administration lead to high levels of patient compliance.

Many patients require quick onset of action in particular therapeutic condition and consequently immediate release of medicament is required. It is estimated that 50% of the population is affected by this problem, which results in a high incidence of ineffective therapy. 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.[1]

Advantages of Immediate Release Drug Delivery System

An immediate release pharmaceutical preparation offers[2]

1. Improved compliance/added convenience
2. Improved stability
3. Suitable for controlled/sustained release actives
4. Allows high drug loading.
5. Ability to provide advantages of liquid medication in the form of solid preparation.
6. Adaptable and amenable to existing processing and packaging machinery
7. Cost- effective

DIFFICULTIES WITH EXISTING ORAL DOSAGE FORM[2]

1. Patient may suffer from tremors therefore they have difficulty to take powder and liquids. In dysphasia physical obstacles and adherence to an Oesophagus may cause gastrointestinal ulceration.
2. Swallowing of solid dosage forms like tablet and capsules and produce difficulty for young adult of incomplete development of muscular and nervous system and elderly patients suffer from dysphasia.
3. Liquid medicaments (suspension and emulsion) are packed in multidose container; therefore achievement of uniformity in the content of each dose may be difficult.

4. Buccal and sublingual formation may cause irritation to oral mucosa, so patients refused to use such medications.

5. Cost of products is main factor as parenteral formulations are most costly and discomfort.

**Salient Features**[3]

- Drugs should possessing long biological half life for immediate release drug delivery.
- The drug is released quickly and completely in one shot.
- High bioavailability expected with immediate release dosage form.
- Lower clearance and lower elimination half life are also requirement for immediate release drug delivery system.
- But main criterion for immediate release dosage form is poor solubility of the drug and need the immediate action of drug to treat unwanted defect or disease.
- Rapid drug therapy intervention is possible.
- New business opportunities like product differentiation, line extension and lifecycle management, exclusively of product promotion.

**Criteria for Drug Selection**[3]

- Poor solubility of the drug and need immediate drug action in case of immediate release dosage form.
- The immediate release compositions comprise micronized drug in an amount sufficient to provide the desired daily dosage, that is, an amount of about 10 mg to about 1000 mg, more preferably an amount of about 20 mg to 400 mg.
- Immediate release compositions from which about 50% of the micronized drug is dissolved in vitro within about 15 minutes, more preferably at least about 80% of the drug is dissolved in vitro within about 30 minutes.
- Carrier materials for immediate release compositions preferably are selected to provide a disintegration time less than about 30 minutes, preferably about 20 minutes or less, more preferably about 18 minutes or less.

**Unsuitable drug characteristic for immediate release tablets**[3]

- Drug are not suitable for immediate release tablets which having short biological half life.
- Drug with low bioavailability are also not desirable candidate for immediate release tablets.
Drug with higher clearance and higher elimination half life are also not desirable candidate for immediate release tablets.

**EXCIPIENTS USED IN IMMEDIATE RELEASE DRUG DELIVERY SYSTEM**

Excipients balance the properties of the actives in immediate release dosage forms. This demands a thorough understanding of the chemistry of these excipients to prevent interaction with the actives. Determining the cost of these ingredients is another issue that needs to be addressed by formulators. The role of excipients is important in the formulation of fast-melting tablets. These inactive food-grade ingredients, when incorporated in the formulation, impart the desired organoleptic properties and product efficacy.

**SUPER DISINTEGRANTS**

A disintegrant is an excipient, which is added to a tablet or capsule blend to aid in the break-up of the compacted mass when it is put into a fluid environment.

**ADVANTAGES**

1. Effective in lower concentrations
2. Less effect on compressibility and flow ability
3. More effective intragranularly.

**Commonly used Super disintegrates are**

**Sodium Starch Glycolate (Explotab, primogel)**

used in concentration of 2-8% and optimum is 4%.

**Mechanism of Action**

Rapid and extensive swelling with minimal gelling.

**Microcrystalline cellulose** (Synonym: Avicel, celex) used in concentration of 2-15% of tablet weight. Water wicking.

**Cross-linked Povidone (crosplvidone)**

(Kollidone) used in concentration of 2-5% of weight of tablet. Completely insoluble in water.
Mechanism of Action
Water wicking, swelling and possibly some deformation recovery. Rapidly disperses and swells in water, but does not gel even after prolonged exposure. Greatest rate of swelling compared to other disintegrants. Greater surface area to volume ratio than other disintegrants.

Low-substituted hydroxyl propyl cellulose
Which is insoluble in water. Rapidly swells in water. Grades LH-11 and LH-21 exhibit the greatest degree of swelling. Certain grades can also provide some binding properties while retaining disintegration capacity. Recommended concentration 1-5%.

Cross linked carboxy methyl cellulose sodium (i.e. Ac-Di-sol) Croscarmellosesodium
Mechanism of Action
Wicking due to fibrous structure, swelling with minimal gelling. Effective Concentrations: 1-3% Direct Compression, 2-4% Wet Granulation.

Conventional Technique Used In The Preparation Of Immediate Release Tablets[5]
Tablet molding technique
Direct compression technique
Wet granulation technique
Solid dispersions technique
Mass extrusion technique

Tablet molding technique[5]
In this technology, water-soluble ingredients are used so that tablet disintegrate and dissolve rapidly. The powder blend is moistened with a hydro 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.
Wet granulation[^6]

Wet granulation is a commonly used unit operation in the pharmaceutical industry. Wet granulation is often carried out utilizing a high-shear mixer. The high-shear granulation process is a rapid process which is susceptible for over wetting. Thus, the liquid amount added is critical and the optimal amount is affected by the properties of the raw materials. Power consumption of the impeller motor and the impeller torque have been applied to monitor the rheological properties of the wet mass during agglomeration and, thereby, have been used to determine the end-point of water addition. However, these methods are affected by the equipment variables. Hence, additional process monitoring techniques would be valuable. Important steps involved in wet granulation.

1. Mixing of drug(s) and excipients.
2. Preparation of binder solution.
3. Mixing of binder solution with powder mixture to form wet mass.
4. Coarse screening of wet mass using a suitable sieve (6-12 screens).
5. Drying of moist granules.
6. Screening of dry granules through a suitable sieve (14-20 screen).
7. Mixing of screened granules with disintegrant, glidant and lubricant.

Limitation of wet granulation.

- The greatest disadvantage of wet granulation is its cost. It is an expensive process because of labor, time, equipment, energy and space requirements.
- Loss of material during various stages of processing.
Stability may be a major concern for moisture sensitive or thermolabile drugs.

An inherent limitation of wet granulation is that any incompatibility between formulation components is aggravated. It is a unique granulation technique that directly converts liquids into dry powder in a single step. This method removes moisture instantly and converts pumpable liquids into a dry powder.

Advantages

- Rapid process.
- Ability to be operated continuously.
- Suitable for heat sensitive product.

![Flow chart](image)

**Fig 2. Wet granulation technique**

**Direct Compression Method**\[^1\]

The term “direct compression” is defined as the process by which tablets are compressed directly from powder mixture of API and suitable excipients. No pretreatment of the powder blend by wet or dry granulation procedure is required. Amongst the techniques used to prepare tablets, direct compression is the most advanced technology. It involves only blending and compression, thus offering advantage particularly in terms of speedy production, as it requires fewer unit operations, less machinery, reduced number of personnel and considerably less processing time along with increased product stability.

Advantages

- Direct compression is more efficient and economical process as compared to other processes, because it involves only dry blending and compaction of API and necessary excipients.
The most important advantage of direct compression is that it is an economical process. Reduced processing time, reduced labor costs, fewer manufacturing steps and less number of equipments are required, less process validation, reduced consumption of power.

- Elimination of heat and moisture, thus increasing not only the stability but also the suitability of the process for thermolabile and moisture sensitive API.
- Particle size uniformity.
- Prime particle dissolution.
- In case of directly compressed tablets after disintegration, each primary drug particle is liberated. While in the case of tablets prepared by compression of granules, small drug particles with a larger surface area adhere together into larger agglomerates; thus decreasing the surface area available for dissolution.

Disadvantages
Excipients Related
- Problems in the uniform distribution of low dose drugs. High dose drugs having high bulk volume, poor compressibility and poor flowability are not suitable for direct compression for example, Aluminium Hydroxide, Magnesium Hydroxide.
- The choice of excipients for direct compression is extremely critical. Direct compression diluents and binders must possess both good compressibility and good flowability.

Solid dispersions technique\[8,9\]
When formulating such solid amorphous dispersions into immediate release solid dosage forms for oral administration to a use environment such as the GI tract of an animal such as a

![Flow chart]

Fig 3. Direct compression technique
human, it is often desirable to maximize the amount of dispersion present in the dosage form. This minimizes the size of the solid dosage form required to achieve the desired dose. Depending on the drug dose, it is often desired that the solid amorphous dispersion comprise at least 30 wt %, preferably at least 50 wt % and more preferably at least 50 wt % or more of the solid dosage form. Such high drug loadings of dispersion in a solid dosage form minimize the dosage form's size, making it easier for the patient to swallow it and tending to improve patient compliance.

**Fig 4. Solid dispersions technique**

**Mass extrusion technique**[10]

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.

**Fig 5. Mass extrusion technique**

**EVALUATION**

**A. Precompression characterization**

1. Bulk density
2. Tapped density
3. Carr’s index
4. Hausner’s ratio
5. Angle of repose

B. Post compression characterization
1. Tablet Dimensions
2. Tablet Hardness
3. Uniformity of Drug Content
4. Weight Variation
5. Friability
6. *In vitro* drug release study (Dissolution Studies)

Precompression characterization

**Bulk density**
Bulk density was determined (Konark instrument) by placing the granules blend in a measuring cylinder and total volume was noted. The weight of granule bed was determined in Schimadzu BL 2200H electronic balance. Bulk density was calculated by using the formula.[11,12]

\[
\text{Bulk density (BD)} = \frac{\text{Total weight of granules}}{\text{Total volume of granules}}
\]

**Tapped density**
Tapped density (TD) was determined (Tapped density apparatus, Konark Instrument) by taking the dried granules in a measuring cylinder and measuring the volume of granules after 100 tapping and weight of total granules.[11,12]

\[
\text{Tapped density} = \frac{\text{Total weight of granules}}{\text{Total volume of granules}}
\]

**Carr’s Index**
The percentage compressibility of a powder was a direct measure of the potential powder arch or bridge strength and stability. The Carr’s index of the powder was determined by using formula.[11,12]

\[
\text{Carr’s index (\%)} = \frac{[(\text{TD-BD}) \times 100]}{\text{TD}}
\]

**Hausner’s ratio**
The ratio of tapped density to bulk density of the powders is called the Hausner’s ratio.[11,12] The Hausner’s ratio was calculated by.

\[
\text{Hausner’s Ratio} = \frac{\text{TD}}{\text{BD}}
\]
Table 1: Specifications of flow properties of granules

<table>
<thead>
<tr>
<th>Carr’s Index</th>
<th>Type of flow</th>
<th>Hausner’s ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 10</td>
<td>Excellent</td>
<td>1.00 – 1.11</td>
</tr>
<tr>
<td>11-15</td>
<td>Good</td>
<td>1.12 – 1.18</td>
</tr>
<tr>
<td>16-20</td>
<td>Fair</td>
<td>1.19 – 1.25</td>
</tr>
<tr>
<td>21-25</td>
<td>Passable</td>
<td>1.26 – 1.34</td>
</tr>
<tr>
<td>26-31</td>
<td>Poor</td>
<td>1.35 – 1.45</td>
</tr>
<tr>
<td>32-37</td>
<td>Very poor</td>
<td>1.46 – 1.59</td>
</tr>
<tr>
<td>≥ 38</td>
<td>Very very poor</td>
<td>≥ 1.60</td>
</tr>
</tbody>
</table>

Angle of Repose
The angle of repose was determined by the funnel method. The accurately 10 gm weighed granules taken in a funnel. Height of the funnel was adjusted such that the tip of the funnel was 6 cm from the graph paper. The powder was allowed to flow through funnel freely onto the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation.\(^7,13,14,11,12\)

\[
\tan \theta = \frac{h}{r}
\]
Therefore, \( \theta = \tan^{-1} \frac{h}{r} \)

Where, \( \theta \) = angle of repose, \( h \) = height of the cone and \( r \) = radius of the cone base.

Table 2: Specifications of angle of repose

<table>
<thead>
<tr>
<th>Angle of repose in degrees</th>
<th>Type of flow</th>
</tr>
</thead>
<tbody>
<tr>
<td>25-30</td>
<td>Excellent</td>
</tr>
<tr>
<td>31-35</td>
<td>Good</td>
</tr>
<tr>
<td>36-40</td>
<td>Fair</td>
</tr>
<tr>
<td>41-45</td>
<td>Passable</td>
</tr>
<tr>
<td>46-55</td>
<td>Poor</td>
</tr>
<tr>
<td>56-65</td>
<td>Very poor</td>
</tr>
<tr>
<td>≥66</td>
<td>Very very poor</td>
</tr>
</tbody>
</table>

Postcompression characterization

Tablet Dimensions
Three tablets of each formulation were randomly selected and there thickness and diameter was measured using digital verniercalliper. Average of three readings was taken and results were tabulated.\(^11,12\)

Tablet Hardness
The crushing strength kg/cm\(^2\) of prepared tablets was determined for 3 tablets by using Monsanto hardness tester. A tablet is placed between the anvils and the crushing strength,
which causes the tablet to break, is recorded. Average of three readings was taken and results were tabulated. The average hardness and standard deviation was determined.\textsuperscript{[11,12]}

**Friability**

Roche friabilator was used for testing the friability. Twenty tablets were weighed accurately and placed in the tumbling apparatus that revolves at 25 rpm for 4 min., the tablets were weighed and the percentage loss in tablet weight was determined.\textsuperscript{[11,12]}

\[
\% \text{ Friability} = \frac{\text{Initial wt. of tablets} - \text{Final wt. of tablets}}{\text{Initial wt. of tablets}} \times 100
\]

**Weight Variation**

Twenty tablets were weighed individually and the average weight was determined. Then percentage deviation from the average weight was calculated. Deviation should not exceed the values given in table (Table 11).\textsuperscript{[11,12]}

**Table 3: Percentage weight variation allowed under weight variation**

<table>
<thead>
<tr>
<th>Average tablet of the tablet (mg)</th>
<th>Percentage deviation</th>
</tr>
</thead>
<tbody>
<tr>
<td>80 mg or less</td>
<td>10</td>
</tr>
<tr>
<td>More than 80 mg but less than 250 mg</td>
<td>7.5</td>
</tr>
<tr>
<td>250 or more</td>
<td>5</td>
</tr>
</tbody>
</table>

**Uniformity of Drug Content**

Weigh and powder 20 tablets, weigh accurately a quantity of powder equivalent to 200 mg TGHH shake with 70 ml methanol and diluted to 100 ml with methanol. Dilute 10 ml of stock and diluted to 100 ml with methanol. Further dilute 10 ml to 100 ml and measure the absorbance at 242.20 nm by taking 798 as \(1\%_{1\text{cm}}\) at the wavelength 242.20 nm.\textsuperscript{[15]}

**In vitro drug release study (Dissolution Studies)**

The release rate of TGHH tablet was determined using USP dissolution testing apparatus II (Paddle type). The test was performed using 900 ml of PBS (pH 1.2) at 37 ± 0.5\(^{\circ}\)C and 50 rpm for 50 min. Samples of 5 ml were withdrawn after suitable time interval (10 min), filtered with Whitman’s filter paper and replaced with 5 ml of fresh dissolution medium. The samples were estimated spectrophotometrically at 242.20nm by using Labindia 3000 UV Spectrophotometer and percentage drug release was calculated.\textsuperscript{[16]}
CONCLUSION

There is a clear opportunity for new enhanced oral products arising within this market segment. This proprietary technology is applicable to a wide range of therapeutic agents including generics, thereby adding value, i.e. ‘supergenerics’ for veterinary or human application. Approximately one-third of the patients need quick therapeutic action of drug, resulting in poor compliance with conventional drug therapy which leads to reduced overall therapy effectiveness. A new dosage format, the immediate release pharmaceutical form has been developed which offers the combined advantages of ease of dosing and convenience of dosing. These tablets are designed to release the medicaments with an enhanced rate. Due to the constraints of the current technologies as highlighted above, there is an unmet need for improved manufacturing processes for immediate release pharmaceutical form that are mechanically strong, allowing ease of handling and packaging and with production costs similar to that of conventional tablets. To fulfil these medical needs, formulators have devoted considerable effort to developing a novel type of tablet dosage form for oral administration, one that disintegrates and dissolves rapidly with enhanced dissolution. An extension of market exclusivity, which can be provided by a immediate release dosage form, leads to increased revenue, while also targeting underserved and under-treated patient populations.

REFERENCE


