IMMEDIATE RELEASE DRUG DELIVERY SYSTEM: A REVIEW

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ABSTRACT
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. As a drug entity nears the end of its patent life, it is common for pharmaceutical manufacturers to develop a given drug entity in a new and improved dosage form. Drug delivery systems (DDS) are a strategic tool for expanding markets/indications, extending product life cycles and generating opportunities. Oral administration is the most popular route for systemic effects due to its ease of ingestion, pain, avoidance, versatility and most importantly, patient compliance. 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. Immediate release solid oral dosage forms are classified as either having rapid or slow dissolution rates. Immediate release dosage forms are those for which ≥85% of labelled amount dissolves within 30 min. For immediate release tablets, the only barrier to drug release is simple disintegration or erosion stage, which is generally accomplished in less than one hour. 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.
Keywords: Immediate release tablet, superdisintegrants, polymers

INTRODUCTION
The task of developing immediate release tablet is accomplished by using a suitable diluents and super-disintegrant. Faster disintegration of the tablet administrated orally minimizes absorption time and improves its bioavailability in less time. Immediate Release tablet of Antibiotic drug is formulated using dry granulation using super disintegrant croscarmellose sodium. One of the important studies included in the present investigation is of study on process parameter effect on performance of the Immediate Release tablets. The effect of selected process parameters on critical properties of immediate release (IR) tablets were studied, like effect of disintegration time, friability, dissolution profile. Many patients especially children and elderly have difficulty in swallowing tablets and capsules and consequently unable to take medicine as prescribed. Almost 50% of the population is affected by such problem, resulting in the high incidence of noncompliance and ineffective therapy. Most pharmaceutical forms for oral administration are formulated for direct ingestion, or for chewing, or for prior dispersion and/or dissolution in water; some of them are absorbed in the mouth (sublingual or buccal tablets). To obviate the problems associated with conventional dosage forms, orally immediate release tablets have been developed, which combine hardness, dosage uniformity, stability and other parameters, with extremely easy administration, since no water is required for swallowing the tablets and they are thus suitable for geriatric, paediatric and traveling patients[1].

Pharmaceutical products designed for oral delivery and currently available on the prescription and over-the-counter markets are mostly the immediate release type, which are designed for immediate release of drug for rapid absorption. 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. Super-disintegrant improves disintegrant efficiency resulting in decreased use levels when compared to traditional disintegrant[2].

Immediate release solid oral dosage forms are classified as either having rapid or slow dissolution rates. Immediate release dosage forms are those for which ≥85% of labelled amount dissolves within 30 min. For immediate release tablets, the only barrier to drug release is simple disintegration or erosion stage, which is generally accomplished in less than one hour1. To enhance dissolution and hence bioavailability of any drug from immediate
release tablets, disintegration is one of the important process. Few Super-disintegrant are available commercially as Croscarmellose sodium, Crospovidone and SSG[3].

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. Direct compression, is one of the techniques that requires the incorporation of a superdisintegrants into the formulation. Direct compression does not require the use of water or heat during the formulation procedure and is very sensitive to changes in the type and proportion of excipients and the compression forces, when used to achieve tablets of suitable hardness without compromising the rapid disintegration characteristics[4].

DEFINITION
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[5]. Thus, the term excludes formulations which are adapted to provide for “modified”, “controlled”, “sustained”, “prolonged”, “extended” or “delayed “release of drug.

Advantages of Immediate Release Drug Delivery System
An immediate release pharmaceutical preparation offers[6]
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
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.

TABLET MANUFACTURING
The manufacturing of oral solid dosage forms such as tablets is a complex multi-stage process under which the starting materials change their physical characteristics a number of times before the final dosage form is produced. Traditionally, tablets have been made by granulation. Both wet granulation and dry granulation or direct compression is used.[7]

Following are the various unit processes which are involved in making tablets.
1. Dispensing
2. Sizing
3. Powder blending
4. Granulation
5. Drying
6. Tablet compression
7. Packaging

Various factors associated with these processes can seriously affect content uniformity, bioavailability or stability.

1. Dispensing (weighing and measuring)
Dispensing is the first step in any pharmaceutical manufacturing process. It is one of the most critical steps in pharmaceutical manufacturing, during this step, the weight of each ingredient in the mixture is determined according to dose.
Dispensing may be done manually by hand scooping from primary containers and weighing each ingredient by hand on a weigh scale, manual weighing with material lifting assistance like vacuum transfer and bag lifters, manual or assisted transfer with automated weighing on weigh table, manual or assisted filling of loss-in weight dispensing system.
2. Sizing
Sizing is a process in which the size of particle is changed/ minimized to promote desired properties in a tablet.

**Advantages of sizing include**
- Improved tablet-to-tablet content uniformity by of increased number of particles per unit weight.
- Controlled particle size distribution to promote better flow of mixture in tablet machine.
- Improved flow properties of materials.
- Improved color and/or active ingredient dispersion in tablet excipients.
- Uniformly sized wet granulation to promote uniform drying.

**Disadvantages**
There are also certain disadvantages associated with this unit operation if not controlled properly.

They are as follows
- A possible change in polymorphic form of the active ingredient, rendering it less or totally inactive, or unstable.
- A decrease in bulk density of active compound and/or excipients, which may cause flow problem and segregation in the mix.
- An increase in surface area from size reduction may promote the adsorption of air, which may inhibit wettability of the drug to the extent that it becomes the limiting factor in dissolution rate.

A number of different types of machines may be used for dry sizing or milling depending on whether gentle screening or particle milling is needed. The ranges of equipment employed for this process includes Fluid energy mill, Colloidal mill, Ball mill, Hammer mill, Cutting mill, Roller mill, etc.

3. Powder Blending
The successful mixing of powder is acknowledged to be more difficult unit operation because, unlike the situation with liquid, perfect homogeneity is practically unattainable. In practice, problems also arise because of the inherent cohesiveness and resistance to movement between the individual particles. The process is further complicated in many
systems, by the presence of substantial segregation influencing the powder mix. They arise because of differences in size, shape, surface morphology, density of the component particles etc. The powder/granules blending is involved at pre granulation and/or post granulation stage of tablet manufacturing. Each process of mixing has optimum mixing time and so prolonged mixing may result in an undesired product. The optimum mixing time and mixing speed are to be evaluated. Blending step prior to compression is normally achieved in a simple blender. The blender may be a fixed blender into which the powders are charged, blended and discharged.

4. Granulation
Granulation may be defined as a size enlargement process which converts small particles into physically stronger & larger agglomerates. The objective of granulation is to improve powder flow and handling, decrease dustiness, and prevent segregation of the constituents.
Granulation method can be broadly classified into two types

(i) Wet granulation and (ii) Dry granulation

Ideal characteristics of granules
The ideal characteristics of granules include spherical shape, smaller particle size distribution with sufficient fines to fill void spaces between granules, adequate moisture (between 1-2%), good flow, good compressibility and sufficient hardness etc.

The effectiveness of granulation depends on the following properties:
- Particle size of the drug and excipients
- Type of binder (strong or weak)
- Volume of binder (less or more)
- Wet massing time (less or more)
- Amount of shear applied
- Drying rate (Hydrate formation and polymorphism)

(i) Wet granulation
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.

**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. Course 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**
1. The greatest disadvantage of wet granulation is its cost. It is an expensive process because of labour, time, equipment, energy and space requirements.
2. Loss of material during various stages of processing.
3. Stability may be a major concern for moisture sensitive or thermolabile drugs.
4. An inherent limitation of wet granulation is that any incompatibility between formulation components is aggravated.

- **Special wet granulation techniques**
  High shear mixture granulation
  Fluid bed granulation
  Extrusion-spheronization
  Spray drying

**(ii) 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.

The more widely used method is slugging, where the powder is precompressed and the resulting tablets or slugs are milled to yield granules.

The other method is to precompress the powder with pressure rolls using a machine such as
Chilosonator.

**Advantages**
The main advantages of dry granulation or slugging are that it uses less equipments and space. It eliminates the need for binder solution, heavy mixing equipment and the costly and time consuming drying step required for wet granulation. Slugging can be used for advantages in the following situations:

- For moisture sensitive material
- For heat sensitive material
- For improved disintegration since powder particles are not bonded together by a binder

**Disadvantages**
- It requires a specialized heavy duty tablet press to form slug.
- It does not permit uniform color distribution as can be achieved with wet granulation where the dye can be incorporated into binder liquid.
- The process tends to create more dust than wet granulation, increasing the potential contamination.

**Steps in dry granulation**
1. Milling of drugs and excipients
2. Mixing of milled powders
3. Compression into large, hard tablets to make slug
4. Screening of slugs
5. Mixing with lubricant and disintegrating agent
6. Tablet compression

**Two main dry granulation processes**

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

(iii) Direct compression
The term “direct compression” is defined as the process by which tablets are compressed directly from powder mixture of API and suitable excipients. No pre-treatment 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 labour costs, fewer manufacturing steps, and less number of equipments is 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, Aluminum 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.
- Many active ingredients are not compressible either in crystalline or amorphous forms.

Process Related

- Capping, lamination, splitting, or layering of tablets is sometimes related to air entrapment during direct compression. When air is trapped the resulting tablets expand when the pressure of tablet is released, resulting in splits or layers in the tablet.
- In some case it requires greater sophistication in blending and compression equipments.

2 List of advancement technique in Granulations

- Steam Granulation
- Melt Granulation / Thermoplastic Granulation
- Moisture Activated Dry Granulation (MADG)
- Moist Granulation Technique (MGT)
- Thermal Adhesion Granulation Process (TAGP)
- Foam Granulation

5. Drying

Drying is a mass transfer process in the removal of water from a solid by evaporation. The essential constituents of an effective piece of drying equipment are heat supply to increase the temperature and thereby reduce relative humidity, a device for removal of evaporated water and a means of minimizing the distance that water molecules must diffuse before they can be evaporated. The fluidized bed drier is the most commonly used device for drying tablet granules. The solid is fluidized from below by a jet of hot air, and so each granule is separated from its neighbouring granules. The air provides an effective means of heat transfer, as well as of removing water vapours. The speed of the drying process is governed by the distance that water molecules must diffuse before they arrive at the evaporative surface. Since the wet granules are present as individual units, the maximum distance over
which diffusion occurs is equal to the radius of a granule. Hence, fluidized bed drying is a rapid process. A more traditional means of drying is the tray drier. Hot air flows over a series of shelves on which the wet material is spread. Compared to the fluidized bed drier, the solid-air interface is smaller, and water molecules may have to diffuse through the whole thickness of the solid layer before the evaporative surface is reached. Thus, the drying process is slower in a tray drier than in a fluidized bed drier.

6. Compression
During compression, the bulk volume of the material is reduced, resulting in the displacement of the gaseous phase. Further increasing the force leads to particle deformation and rearrangement.

DESIRED CRITERIA FOR IMMEDIATE RELEASE DRUG DELIVERY SYSTEM[8]
Immediate release dosage form should- In the case of solid dosage it should dissolve or disintegrate in the stomach within a short period.
1. In the case of liquid dosage form it should be compatible with taste masking.
2. Be portable without fragility concern.
3. Have a pleasing mouth feel.
4. It should not leave minimal or no residue in the mouth after oral administration.
5. Exhibit low sensitivity to environmental condition as humidity and temperature.
6. Be manufactured using conventional processing and packaging equipment at low cost.
7. Rapid dissolution and absorption of drug, which may produce rapid onset of action.

Evaluation of immediate release tablets[9]
A) Evaluation Of Blend:
The prepared blend is evaluated by following tests.
1. Angle of repose
2. Bulk density
3. Tapped density
4. Carr’s index
5. Hauser’s ratio

1. 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)-excipient 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.

\[ \tan \theta = \frac{h}{r} \]

2. 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 \( (V_0) \). Calculate the apparent bulk density in gm/ml by the following formula-

**Bulk density = Weight of powder / Bulk volume**

3. 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 \( (V_1) \) to the nearest graduated units, repeat the tapping an additional 750 times and measure the tapped volume \( (V_2) \) to the nearest graduated units. If the difference between the two volumes is less than 2% then final the volume \( (V_2) \). Calculate the tapped density in gm/ml by the following formula-

**Tapped density = Weight of powder / Tapped volume**

4. 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= \( [(TD-BD) \times 100] / TD \)**

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

**Hausner’s ratio = TD/BD**

**B) Physical parameters**

1. **Hardness**

   Tablets require certain amount of strength or hardness and resistance to friability, to withstand mechanical shocks of handling in manufacture, packaging, and shipping. The most widely used apparatus to measure tablet hardness (crushing strength) is the Schleuniger hardness tester.

2. **Friability**

   Friability is related to tablets ability to withstand both shocks and abrasion without crumbling during manufacturing, packing, transportation and consumer handling. Friability can be evaluated by means of friability test apparatus. Acceptable limit was not more than 1.0% of three samples.

   **Method:** Accurately weighed 6.5 gm of tablet and transfer into Friabilator and subjected to 100 revolutions in 4 minutes. Dedusted tablets were reweighed (final wt).

   \[
   \text{% friability} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100
   \]

3. **Thickness**

   Ten tablets were selected at random from individual formulations and thickness was measured by using Vernier-caliper scale, which permits accurate measurement.

**REFERENCES**


