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### IMMEDIATE DRUG RELEASE TABLETS: A REVIEW

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#### **ABSTRACT:**

Immediate release dosage form has emerged as alternative oral dosage forms. Immediate drug release dosage forms disintegrate rapidly after administration with enhanced rate of dissolution. The basic approach used in development of tablets is the use of superdisintegrants like Cross linked Polyvinylpyrrolidone or Crosspovidone (Polyplasdone), Sodium starch glycolate (Primogel, Explotab), Carboxymethylcellulose (Croscarmellose) etc. These superdisintegrants provide instantaneous disintegration of tablet after administration in stomach. Among all dosage forms, tablet is the most popular dosage form existing today because of its convenience of self administration, compactness and easy manufacturing; sometimes immediate onset of action is required than conventional therapy in many cases. In this field immediate release liquid dosage forms and parenteral dosage form have also been introduced for treating patients. In liquid dosage form can be suspensions with typical dispersion agents like hydroxypropyl methylcellulose, AOT (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., neuroleptics, cardiovascular drugs, analgesics, antihistamines and other drugs can be considered candidates for this dosage form. 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.

**Keywords:** Immediate release tablets, Superdisintegrants, Polymers, Oral dosage form.

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#### **INTRODUCTION**

Solid dosage form is one of the most popular pharmaceutical forms contain active and inactive ingredients, in which the drug present in prescribed amount, so it is more accurate, stable and easier to administer to patient, i.e. it is more convenient for administration. But in the present study and research novel drug delivery systems are developed for expanding markets. Oral administration is the most popular route for systemic effects due to its ease of ingestion, pain avoidance, versatility and most importantly patient compliance. In these solid formulations 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. Many patients require quick onset of action in particular therapeutic condition and consequently

immediate release of medicament is required. The developments 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<sup>1</sup>.

#### **Pharmaceutical Tablets**

Because oral administration of drug is simple, convenient and safe, it is the most frequently used route. At least 90% of drug used to produce systemic effects are administered orally<sup>2</sup>.

The European Pharmacopoeia (2002) defines tablets as solid preparation each containing a single dose of one

or more active substances and usually obtained by compressing uniform volumes of particles. Tablets are intended for oral administration. Some are swallowed whole, some after being chewed, some are dissolved or dispersed in water before being administered and some are retained in the mouth where the active substances is liberated. Despite the long and continuing history of the development of new technologies for administration of drugs, the tablet form remains the most commonly used dosage form<sup>3</sup>.

#### **Classification of Tablets**

Based on their drug-release characteristics, tablets can be classified into:

**a) Immediate Release Tablets:** In immediate release tablets the drug is intended to be released rapidly after administration, or the tablet is dissolved and administered as a solution. This is the most common type of tablets and includes: disintegrating, chewable, effervescent, lozenges, sublingual and buccal tablets.

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. This term excludes formulations which are adapted to provide for "modified", "controlled", "sustained", "prolonged", "extended" or "delayed" release of drug<sup>4</sup>.

**b) Modified Release Tablets:** In contrast to conventional tablets or tablets for instant release, modified release tablets can provide a range of release patterns (extended, delayed or repeated release) resulting in deposition of the drug in varying positions within the gastrointestinal tract. Several alternative terms are used to describe extended release systems, such as controlled release, prolonged release and sustained release. The release rate or time to release onset differ among the modified release tablet systems, but the main common objective is to control the release of the drug from the dosage form. The main mechanisms that can be controlled are the dissolution of the active substance and the diffusion of the dissolved drug within the tablet. There are several techniques available to accomplish this. A dissolution controlled release system can be obtained by covering the readily soluble drug particles and the tablets with slowly soluble coatings. It is also possible to modify the structure of the active substance to reduce its solubility, resulting in a slower dissolution rate. The diffusion can be controlled by the addition of an insoluble membrane surrounding the drug particles or the tablets or by forming matrix tablets. In the latter, the active substance dissolves within the tablet and diffuses through the membrane or

matrix. The drug can also be incorporated into an ending matrix; the drug is then released as the matrix erodes and also by diffusion process within the matrix<sup>5</sup>.

#### **Advantages and Disadvantages of Immediate Release Tablets**

##### **Advantages**

- a) Economical and cost effective.
- b) Quick onset of action.
- c) Suitable for industrial production.
- d) Improved stability and bioavailability.
- e) Provides some advantages of liquid dosage forms.
- f) Adaptable and amendable to existing processing and packaging machinery.
- g) Unique product differentiation.

##### **Disadvantages**

- a) Rapid drug therapy intervention is not possible.
- b) Sometimes may require more frequency of administration.
- c) Dose dumping may occur.
- d) Reduced potential for accurate dose adjustment.

**Drug Release:** Immediate release dosage forms are designed to allow drugs to dissolve freely in the gut contents, with no intention of delaying or prolonging dissolution or absorption of the drugs upon administration. Immediate release products could be rapidly-dissolving or slowly-dissolving, depending on the intrinsic dissolution rate of drug substances<sup>6</sup>.

**Excipients:** 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. Excipients are general and can be used for a broad range of actives, except some actives that require masking agents.

**Super Disintegrants:** A disintegrant is an excipient, which is added to a tablet or capsule blend to aid in the breakup of the compacted mass when it is put into a fluid environment. **Advantages:**

- Effective in lower concentrations
- Less effect on compressibility and flowability
- More effective intragranularly

**Some super disintegrants are:**

**1. Sodium Starch Glycolate (Explotab, primogel)** used in concentration of 2-8% & 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. And Water wicking.

**2. Cross-linked Povidone or crospovidone (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.

**3. 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 is 1-5%.

**4. Cross linked carboxy methyl cellulose sodium (Ac-Di-sol) Crosscarmellose sodium:**

**Mechanism of Action:** Wicking due to fibrous structure, swelling with minimal gelling. Effective Concentrations: 1-3% Direct Compression, 2-4% Wet Granulation<sup>7</sup>.

**Conventional Technique Used in the Preparation of Immediate Release Tablets:**

- Direct Compression Method
- Wet Granulation Method
- Dry Granulation Method

**Direct Compression Method**

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 pre-treatment 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<sup>8</sup>.

**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**

1. The active ingredient and excipients are weighed and mixed.
2. 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 cornstarch, natural gums such as acacia, and cellulose derivatives such as methyl cellulose, gelatin, and povidone.
3. Screening the damp mass through a mesh to form pellets or granules.
4. Drying the granulation. A conventional tray-dryer or fluid-bed dryer are most commonly used.
5. 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<sup>9</sup>.

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<sup>9</sup>.

**Dry Granulation Method**

Dry granulation processes create granules by light compaction of the powder blend under low pressures. The compacts so-formed are broken up gently to produce granules (agglomerates). This process is often used when the product to be granulated is sensitive to moisture and heat. Dry granulation can be conducted on a tablet press using slugging tooling or on a roll press called a roller compactor. Dry granulation equipment offers a wide range of pressures to attain proper densification and granule formation. It is simpler than wet granulation, therefore the cost is reduced. However, this method often produces a higher percentage of fine granules, which can compromise the quality or create yield problems for the tablet. Dry granulation requires drugs or excipients with cohesive properties, and a 'dry binder' may need to be added to the formulation to facilitate the formation of granules. At last powdered lubricants are added<sup>10</sup>.

**Evaluation of powder blend:**

The prepared blend is evaluated by following tests.

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

### 1. Angle of Repose

The angle of repose of API powder was determined by funnel method. Accurately weighed powder blend was taken in a funnel. Height of the funnel was adjusted in such ways that tip of the funnel just touches the apex of the powder blend. The powder blend was allowed to flow through the funnel freely onto the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation:

$$\theta = \tan^{-1} h / r$$

Where,  $h$  and  $r$  are the height and radius of the powder cone<sup>11</sup>.

### 2. Bulk Density

Weight accurately 50 gm of the drug, which is previously passed through 20# sieve and transferred in 100 ml graduated cylinder. Calculate the apparent bulk density in gm/ml by the following formula:

$$\text{Bulk Density} = \text{Weight of powder} / \text{Bulk volume} \\ = w / v$$

### 3. Tapped Bulk Density

Accurately weighed 50 gm of the drug, which was previously passed through 20# sieve and transferred in 100 ml graduated cylinder. Initial volume was observed. The cylinder was tapped initially 100 times and measured the tapped volume to the nearest graduated units.

Calculate the tapped bulk density in gm/ml by the following formula:

$$\text{Tapped density} = \text{weight of the powder} / \text{Tapped volume} \\ = w / v$$

### 4. Hausner's Ratio

The Hausner's ratio is a number that is correlated to the flowability of a powder or granular material.

$$\text{Hausner's ratio} = \text{Tapped density} / \text{Bulk density}$$

### 5. 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 bulk density and tapped density of a powder and the rate at which it packed down. The formula for Carr's Index is as below:

$$\text{Carr's Index (\%)} = [(TBD-LBD) \times 100] / TBD$$

### Evaluation of the formulated tablets.

- Thickness
- Hardness
- Friability
- Weight variation
- Drug content
- Disintegration time
- *In vitro* Drug release study

**1. Thickness:** The thickness of the tablets was determined by using vernier calipers. Randomly 10

tablets selected were used for determination of thickness that expressed in Mean  $\pm$  SD and unit is mm.

**2. Hardness:** The hardness of tablet is an indication of its strength against resistance of tablets to capping, abrasion or breakage under conditions of storage, transportation and handling before usage. Measuring the force required to break the tablet across tests it. Hardness of 10 tablets (randomly) from whole tablet batch was determined by Monsanto hardness tester. Hardness measured in kg/cm<sup>2</sup>.

**3. Friability test:** 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. For tablets with an average weight of 0.65 g or less take a sample of whole tablets corresponding to about 6.5 g and for tablets with an average weight of more than 0.65 g take a sample of 10 whole tablets. Roche friabilator is rotated at 25rpm for 4 minutes for 100 rounds. The tablets were dedusted and weighed again. The percentage of weight loss was calculated using the formula

$$\% f = (w_0 - w_1) \times 100 / w_0$$

Here, % f = Percentage friability W<sub>0</sub> = Initial weight (Before test) W<sub>1</sub> = Final weight (After test).

**4. Weight variation:** The weight variation test is carried out in order to ensure uniformity in the weight of tablets in a batch. The total weight of 20 tablets randomly from whole batch was determined and the average was calculated. The individual weights of the tablets were also determined accurately and the weight variation was calculated.

**5. Drug content:** 10 tablets were powdered and 100mg drug equivalent powder dissolved in suitable media buffer or 0.1N HCl. Volume of the solution made up to 100ml by that media. Solution was filtered and diluted 100times and analyzed spectrophotometrically and further calculation carried out to determine drug content in one tablet.

**6. Disintegration time:** The USP device to rest disintegration was six glass tubes that are "3 long, open at the top, and held against 10" screen at the bottom end of the basket rack assembly. One tablet is placed in each tube and the basket rack is poisoned in 1 L beaker of distilled water at 37 $\pm$ 2°C, 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<sup>12</sup>.

**6. In vitro drug release studies:** The immediate release tablets are subjected to in vitro drug release studies in pH 6.8 phosphate buffer or 0.1N HCl for 30 minutes to access the ability of the formulation for providing

immediate drug delivery. Drug release studies were carried out in dissolution test apparatus using specified volume 900ml of dissolution media maintained at  $37\pm 2^{\circ}\text{C}$ . The tablets are kept in the cylindrical basket or directly placed in medium with paddle then rotated at 100 rpm. 5ml of the sample from the dissolution medium are withdrawn at each time interval (5, 10, 15 & 30 minutes) and 5ml of fresh medium was replaced each time. The samples were filtered and from the filtrate 1ml was taken and diluted to 10 ml. These samples were analyzed spectrophotometrically and further calculation was carried out to get drug release. The drug released data were plotted and tested with zero order (Cumulative % drug released Vs time), First order (Log % Remained Vs time). The in vitro dissolution kinetic parameters, dissolution rate constants, correlation coefficient and dissolution efficiency were calculated<sup>13</sup>.

#### CONCLUSION

This is new enhanced oral product arising within this market segment and applicable to a wide range of therapeutic agents. Approximately one-third of the

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