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Review Article

A Review on Immediate Release Drug Delivery Systems

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ABSTRACT

The oral drug delivery system which includes the solid dosages form such as conventional dosages form and immediate release dosages form. Form last several decades conventional dosage forms like capsule, solid, pills, powder, solution, emulsion, suspension aerosols are used in the various treatments of acute or chronic disease. Today this formulation can be considered as primary pharmaceutical product are mostly seen in overalls market. Tablet is most popular among the all dosages forms today and recently found mostly accepted tablet dosages forms. Because of its convenience easy to administration, convenience of self administration, compactness and easy for the manufacturing. In number of cases immediate onset of action is required than conventional therapy. The basic approach used in development immediate release solid dosages form by using superdisintegrant like sodium starch glycolate (Primogel, Explotab), Polyvinylpyrrolidone (PVP) etc. which provides in instantaneous disintegration of tablet after administration. By using various techniques in can be formulate like wet granulation, direct compression etc. Hence its having A new dosage form allows a manufacturer to extend market exclusivity, while offering its patient population a more convenient dosage form or dosing regimen.

While development if immediate release therapy also provides an opportunity for a line extension in the marketplace, wide range this dosage form. As a drug entity nears the end of its patent life, it is common for pharmaceuticals manufacturer to extend to development a given drug entity in a new and improved dosage form. A new dosage form slows a manufacturer to extend market exclusivity, white offering its patient population a more convenient dosages form or dosing regimen.

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.

Tablets were prepared by wet granulation method using fast releasing excipients such as and superdisintegrant sodium starch glycolate (SSG).

Keywords: immediate release, superdisintegrant, Explotab, PVPK, Conventional Technique

INTRODUCTION [1-6]

Oral drug delivery system includes conventional dosage form and immediate release dosage form. For last so many decades' conventional dosage forms like tablets, capsules, pills, powders, solutions, emulsions, suspensions and aerosols are used in the treatment of acute or chronic diseases. Even today these formulations can be considered as primary pharmaceutical product commonly seen in market.

When such a conventional dosage form is administrated, the concentration of such drug in systemic circulation gradually rises to attend a therapeutic range and this concentration is

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maintained for some time and finally decreases to sub therapeutic value rendering the drug pharmacologically inactive. Each individual drug has a maximum safe concentration and a minimum effective concentration. Fluctuations in plasma concentration may mean that drug levels may swing too high leading to toxic/side effects; alternatively drug may fall too low leading to a lack of efficacy. Furthermore, the plasma drug concentration in a patient at a particular time depends on the compliance with the prescribed dosage interval. Hence, the design of effective drug delivery systems has recently become an integral part of the development of new medicines. The goal is to provide a therapeutic quantity of medicine/s to the proper site in the body in order to achieve the desired effect and maintain such effect for the entire period of treatment. A new development namely, immediate release dosage forms, has evolved from the need for a prolonged drug effect, a better control of drug administration and the reduction of side-effects.

Novel drug delivery systems are developed 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. 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. 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. 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. 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.

INTRODUCTION TO IMMEDIATE RELEASE TABLETS [7-8, 10]

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. This term excludes formulations which are adapted to provide for “modified”, “controlled”, “sustained”, “prolonged”, “extended” or “delayed” release of drug.

Release term includes the provision (or presentation) of drug from the formulation to the gastrointestinal tract, to body tissues and/or into systemic circulation. For gastrointestinal tract release, the release is under pH conditions such as pH=1 to 3, especially at, or about, pH=1.

Biopharmaceutics consideration: [7-8]

When new drug delivery system put on, it is must those to consider Biopharmaceutical factor like metabolism and excretion.

Pharmacokinetics:

In this consideration, study has done absorption, distribution, metabolism and excretion. After absorption, drug attains

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therapeutic level and therefore elicits pharmacological effect, so both rate and extend of absorption is important. In conventional dosages form there is delay in disintegration and therefore dissolution is fast. Drug distribution depends on many factors like tissue, disease state, drug interaction etc.

Duration and intensity of action depends upon rate of drug removal from the body or site of action i.e. biotransformation. Decrease in liver volume, regional blood flow to liver reduces the biotransformation of drug through oxidation, reduction and hydrolysis. Excretion by renal clearance is slowed, thus half– life of renal excreted drug increase.

Pharmacodynamic:

· Drug reception interaction impaired in elderly as well as in young adult due to undue development of organ.

· Decreased ability of the body to respond reflexive stimuli, cardiac output, and orthostatic hypotension may see in taking antihypertensive like Prazosin.

· Decreased sensitivity of the CVS to adrenergic agonist and antagonist.

· Immunity is less and taken into consideration while administered antibiotics.

· Altered response to drug therapy-elderly show diminished bronchodilator effect of theophylline shows increased sensitivity to barbiturates.

· Altered response to drug therapy-elderly show diminished bronchodilator effect of theophylline shows increased sensitivity to barbiturates.

· Concomitant illnesses are often present in elderly, which is also taken into consideration, while multiple drug therapy prescribed.

· Research workers have clinically evaluated drug combination for various classes, cardiovascular agents, diuretics, antihypertensive etc. For immediate release dosages forms. The combination of two or three drug combination choice depends on disease state of the patient.

Problems with Existing Oral Dosage Form: [7-8]

· Patient may suffer from tremors therefore they have difficulty to take powder and liquids. In dysphasia physical obstacles and adherence to an esophagus may cause gastrointestinal ulceration.

· 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.

· Liquid medicaments (suspension and emulsion) are packed in multidose container; therefore achievement of uniformity in the content of each dose may be difficult.

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

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

Criteria for immediate release drug delivery system:

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.

· It should not leave minimal or no residue in the mouth after oral administration.

· Exhibit low sensitivity to environmental condition as humidity and temperature.

· Be manufactured using conventional processing and packaging equipment at low cost.

· Rapid dissolution and absorption of drug, which may produce rapid onset of action.

Merits of Immediate Release Drug Delivery System: [7-8]

· Improved compliance/added convenience.

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· Ability to provide advantages of liquid medication in the form of solid preparation.
· Adaptable and amenable to existing processing and packaging machinery.
· Cost- effective.
· Improved solubility of the pharmaceutical composition.
· Decreased disintegration and dissolution times for immediate release oral dosage forms

Challenges to Develop IRDDS

· It should dissolve or disintegrate in the stomach within a short period.
· Be portable without fragility concern.
· Have a pleasing mouth feel.
· Should not leave minimal or no residue in the mouth after oral administration.
· Should exhibit low sensitivity to environmental condition as humidity and temperature.
· Be manufactured using conventional processing and packaging equipment at low cost.
· Rapid dissolution and absorption of drug, which may produce rapid onset of action.

TABLET EXCIPIENTS AND THEIR FUNCTIONALITIES: [2, 6-13, 17,18,20]

Excipients play a crucial role in design of the delivery system, determining its quality and performance. Excipients though usually regarded as nontoxic there are examples of known excipient induced toxicities which include renal failure and death from diethylene glycol, osmotic diarrhea caused by ingested Mannitol, hypersensitivity reactions from lanolin and cardio toxicity induced by propylene glycol.

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.

In addition to active ingredients, tablet contains a number of inert materials known as additives or excipients

Different excipients are:

1. Diluent
2. Binder and adhesive
3. Disintegrants
4. Lubricants and glidants
5. Colouring agents
6. Flavoring agents
7. Sweetening agents.

1. Diluent:

Diluents are fillers used to make required bulk of the tablet when the drug dosage itself is inadequate to produce the bulk. Secondary reason is to provide better tablet properties such as improve cohesion, to permit use of direct compression manufacturing or to promote flow.

A diluent should have following properties:

1. They must be non toxic.
2. They must be commercially available in acceptable grade.
3. There cost must be low.
4. They must be physiologically inert.
5. They must be physically & chemically stable by themselves & in combination with the drugs.
6. They must be free from all microbial contamination.
7. They do not alter the bioavailability of drug.
8. They must be color compatible.

Commonly used tablet diluents:

1. Lactose-anhydrous and spray dried lactose, lactose monohydrate
2. Directly compressed starch-Sta Rx 1500
3. Hydrolyzed starch-Emdex and Celutab
4. Microcrystalline cellulose-Avicel (PH 101and PH 102)
5. Dibasic calcium phosphate dehydrate
6. Calcium sulphate dihydrate

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7. Mannitol
8. Sorbitol
9. Sucrose- Sugartab,
10. Dextrose

Lactose:
Most widely used diluent in tablet formulation. Lactose has no reaction with most drugs, whether it is used in hydrous or anhydrous form. Anhydrous lactose has advantage over lactose that it does not undergo Maillard reaction which is browning & discoloration of tablet due to the interaction of amine drug with lactose. Spray dried lactose in concentration 20-25% of active ingredient is used for direct compression.

Microcrystalline cellulose: Microcrystalline cellulose, having trade name Avicel is used for direct compression. These are two types: PH-101 (Powder) and PH-102 (Granules). Dibasic calcium phosphate and calcium sulphate used as diluents but reduce bioavailability of tetracycline tablet.

2. Binders:
Binders are adhesives that are added to solid dosage formulations. The primary role of binders is to provide the cohesiveness essential for the bonding of the solid particles under compaction to form a tablet. In a wet-granulation process, binders promote size enlargement to produce granules and thus improve flowability of the blend during the manufacturing process. Binders may also improve the hardness of the tablets by enhancing intragranular as well as intragranular forces. In a direct compression process, binders often act as fillers and impart compressibility to the powder blend.
The cohesive properties of binders may reduce friability of the tablets and thus aid in their durability and elegance. Although the purpose of using binders in a tablet formulation is not to influence its disintegration and dissolution rate, these properties may be modified due to the altered wettability of the formulation.

Liquid Binder:
Wet granulation offers an opportunity for the transformation of crystal forms and the choice of the liquid binder plays an important role in determining the final crystal form of the drug in the granules obtained .Transformation usually occurs during the addition of liquid binder to the powder mass during wet massing and drying of the formed granules. Addition of the binder could be viewed as suspending drug in a mixture of solvent and additives, hence, encouraging transformation of anhydrates to solvated forms. If sufficient liquid binder is added, this could be viewed as a solution step and subsequent drying of granules as the recrystallization step. Thus, close attention has to be paid to polymorph conversion during wet granulation.

Example:
Acacia, tragacanth- Solution for 10-25% concentration Cellulose derivatives- Methyl cellulose, Hydroxy propyl methyl cellulose, Hydroxy propyl cellulose ,Gelatin- 10-20% solution , Glucose- 50% solution ,Polyvinylpyrrolidone (PVP)- 2% conc. ,Starch paste-10-20% solution ,Sodium alginate ,Sorbitol.

3. Disintegrants:
Added to a tablet formulation to facilitate its breaking or disintegration when it contact in water in the GIT. Example: Starch- 5-20% of tablet weight.
Starch derivative – Primogel and Explotab (1-8%) Clays- Veegum HV, bentonite 10% level in colored tablet only Cellulose derivatives- Ac- Di-Sol (sodium carboxy methyl cellulose) Alginate PVP (Polyvinylpyrrolidone), cross-linked.

Superdisintegrants:

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The addition of disintegrant is to facilitate the breakup of tablet, thus presenting the micronized drug to the dissolution medium. In general, for a drug having solubility of 10 mg/mL or less, disintegration rate of the solid dosage form has a profound effect on the dissolution profile. Some of the common superdisintegrants are crospovidone, croscarmellose sodium, and sodium starch glycolate.

Swells up to ten fold within 30 seconds when contact water. Example: Crosscarmellose- cross-linked cellulose, Crosspovidone- cross-linked povidone (polymer), Sodium starch glycolate- cross-linked starch. These cross-linked products swell upto 10n fold within 30 seconds when in contact with water.

Explotab Sodium starch glycolate:

(Sodium starch glycolate) is a partially substituted eat-boxymethyl starch consisting of granules that absorb water rapidly and swell. The mechanism by which this action takes place involves accelerated absorption of water leading to an enormous increase in volume of granules. This results in rapid and uniform tablet disintegration. Explotab is official in the N.F. XVI.

4. Lubricant and Glidants:

Lubricants are intended to prevent adhesion of the tablet materials to the surface of dies and punches, reduce inter particle friction and may improve the rate of flow of the tablet granulation.

Glidants

Are intended to promote flow of granules or powder material by reducing the friction between the particles.

Example: Lubricants- Stearic acid, Stearic acid salt - Stearic acid, Magnesium stearate, Talc, PEG (Polyethylene glycols), Surfactants Glidants- Corn Starch – 5-10% conc., Talc-5% conc., Silica derivative - Colloidal silica such as Cab-O-Sil, Syloid, Aerosil in 0.25-3% conc.

5. Coloring agent:

The use of colors and dyes in a tablet has three purposes:

(1) Masking of off color drugs

(2) Product Identification

(3) Production of more elegant product

All coloring agents must be approved and certified by FDA. Two forms of colors are used in tablet preparation – FD &C and D & C dyes. These dyes are applied as solution in the granulating agent or Lake Form of these dyes. Lakes are dyes absorbed on hydrous oxide and employed as dry powder coloring. Example: FD & C yellow 6-sunset yellow.

6. Flavoring agents:

For chewable table flavor oil are used.

7. Sweetening agents:

For chewable tablets: Sugar, Mannitol, and Saccharine (artificial): 500 times sweeter than sucrose.

FORMULATION ASPECTS IN DEVELOPING IRDDS: [2-3, 7-8, 10,17,18]

Following are the Conventional techniques used in the preparation of immediate release tablets. Conventional Technique Used in the Preparation of Immediate Release Tablet is as below:

1. Tablet molding technique
2. Mass extrusion technique
3. By solid dispersions
4. Direct compression technique
5. Wet granulation technique.

1. Tablet Molding:

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

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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.

2. 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.

3. By solid dispersions:

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 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 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.

The immediate release dosage forms containing a solid dispersion that enhances the solubility of a "low-solubility drug," meaning that the drug may be either "substantially water-insoluble," which means that the drug has a minimum aqueous solubility at physiologically relevant pH (e.g., pH 1-8) of less than 0.01 mg/mL, "sparingly water-soluble," that is, has an aqueous solubility up to about 1 to 2 mg/mL, or even low to moderate aqueous-solubility, having an aqueous-solubility from about 1 mg/mL to as high as about 20 to 40 mg/mL.

The drug dispersions used in fabricating the high loading immediate release dosage forms of the present invention comprise solid dispersions of a drug and at least one concentration-enhancing polymer. The concentration-enhancing polymer is present in the dispersions used in the present invention in a sufficient amount so as to improve the concentration of the drug in a use environment relative to a control composition. At a minimum, the dispersions used in the present invention provide concentration enhancement relative to a control consisting of crystalline drug alone. Thus, the concentration-enhancing polymer is present in a sufficient amount so that when the dispersion is administered to a use environment, the dispersion provides improved drug concentration relative to a control consisting of an equivalent amount of crystalline drug, but with no concentration-enhancing polymer present.

4.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 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

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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.

Direct compression:

Processing steps are:

Figure: 1 Direct Compression Processing Steps

Advantages:

· Low labour input
· A dry process
· Fewest processing steps

Disadvantages:

· Stratification may occur due to differences in particle size and bulk density which results poor content uniformity.
· A large dose drug may cause problem in direct compression. It requires diluents. The tablet becomes large in size which is difficult to swallow and also costly.
· During handling of dry materials static charge may form which may present uniform distribution of drug.
· Direct compression diluent may interact with the drug. For example, amine drug with Lactose produce discoloration of tablet.

5. 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.

Processing steps in wet granulation:

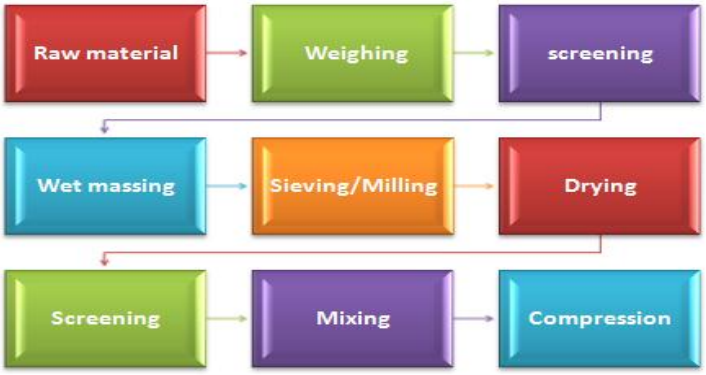

Figure: 2 Wet Granulation Processing Steps

Procedure:

Step 1: The active ingredient and excipients are weighed and mixed.

Step 2: The wet granulate is prepared by adding the liquid binder–adhesive to the powder blend and mixing thoroughly. Examples of

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binders/adhesives include aqueous preparations of cornstarch, natural gums such as acacia, and cellulose derivatives such as methyl cellulose, gelatin, and povidone.

Step 3: Screening the damp mass through a mesh to form pellets or granules.

Step 4: Drying the granulation. A conventional tray-dryer or fluid-bed dryer are most commonly used.

Step 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.

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.

If the granulation is over wetted the granules will be hard, if not wetted sufficiently, the resulting granules will be too soft, breaking down during lubrication. The wet mass is forced through a 6 or 8 mesh (Mesh no. is the number of wires passing through an inch) screen or several mills can be used.

Advantages of Wet Granulation:

· The cohesiveness and compressibility of powders is improved due to the added binder that coats the individual powder particles, causing them to adhere to each other so they can be formed into agglomerates called granules. By this method, properties of the formulation components are modified to overcome their tableting deficiencies. During the compaction process, granules are fractured exposing fresh powder surfaces. Which also improves their compressibility?

· Lower pressures are therefore needed to compress tablets resulting in improvements in tooling life and decreased machine wear.

· Drugs having a high dosage and poor flow and/or compressibility must be granulated by the wet method to obtain suitable flow and cohesion for compression. In this case, the proportion of the binder required to impart adequate compressibility and flow is much less than that of the dry binder needed to produce a tablet by- direct compression.

· Good distribution and uniform content for soluble, low-dosage drugs and color additives are obtained if these are dissolved in the binder solution. This represents a distinct advantage over direct compression where the content uniformity of drugs and uniform color dispersion can be a problem.

· A wide variety of powders can be processed together in a single batch and in so doing their individual physical characteristics are altered to facilitate tableting.

· Bulky and dusty powders can be handled without producing a great deal of dust and airborne contamination.

· Wet granulation prevents segregation of components of a homogeneous powder mixture during processing, transferring, and handling.

· In effect, the composition of each granule becomes fixed and remains the same as that of the powder mixture at the time of the wetting.

· The dissolution rate of an insoluble drug may be improved by wet granulation with the proper choice of solvent and binder.

· Controlled release dosage forms can be accomplished by the selection of a suitable binder and solvent.

Limitations of Wet Granulation:

The greatest disadvantage of wet granulation is its cost because of the space. Time and equipment involved. The process is labor-intensive as indicated by the following.

· Because of the large number of processing steps, it requires a large area with temperature and humidity control.

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· It requires a number of pieces of expensive equipment.
· It is time consuming, especially the wetting and drying steps.
· There is a possibility of material loss during processing due to the transfer of material from one unit operation to another.
· There is a greater possibility of cross-contamination than with the direct-compression method.
· It presents material transfer problems involving the processing of sticky masses.
· It can slow the dissolution of drugs from inside granules after tablet disintegration if not properly formulated and processed.

EVALUATION OF PRE-COMPRESSION PROPERTIES/ POWDER BLEND: [2-3, 7-8, 10, 14]

Precompression characterization of API and granules:

A pre- formulation activity ranges from supporting discovery identification of new active agents to characterizing physical properties necessary for the design of dosage form. Critical information provided during pre formulation can enhance the rapid and successful introduction of new therapeutics entities for humans. Pre-formulation testing is an investigation of physical and chemical properties of a drug substance. The overall objective of pre-formulation testing is to generate information useful in developing the formulation which is stable and bio-available. Further the use of Pre-formulation parameters maximizes the chances in formulating an acceptable, safe, efficacious and stable product. For any drug substances to formulate into a dosage form, it is necessary to study the physicochemical properties of the bulk drug like physical appearance, solubility, bulk density, tapped density, compressibility, melting point, molecular weight, sieve analysis, angle of repose

Table: 1 Limits for Angle of Repose According to I.P.

Angle of repose:

Angle of repose is defined as the maximum angle possible between the surface of pile of powder and the horizontal plane. The granule mass should be allowed to flow out of the funnel orifice on a plane paper kept on the horizontal surface. This forms a pile of granules on the paper.

The angle of repose was determined by the funnel method. The accurately weighed powder was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touched the apex of the heap of the powder. The powder was allowed to flow through the funnel freely onto the surface. The diameter of the powder cone was measured. The angle of repose was calculated by substituting the values of the base radius 'R' and pile height 'H' in the following equation

$$\tan^{-1}\theta = \frac{H}{R}$$

Therefore;

$$\theta = \tan^{-1}\frac{H}{R}$$

Where, θ is angle of repose:
h= height of the pile
r = radius of the pile

Method: weighed quantity of granules was poured through the funnel from the fixed height (23cm) onto the graph paper until the heap of pile of powder touch the tip of funnel. The circumference of the heap was marked by pencil. The radius of circle formed was calculated and angle of repose then calculate on the parameter r which was found out from the radius of circle and height of the heap.

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Sr.No	Angle Of Repose (θ)	Property/type of flow
1	<20	Excellent
2	25-30	Good
3	30-40	Fair passable
4	>40	Very poor

Bulk density (BD):
It is the ratio between a given mass of powder and its bulk volume.

$$\textbf{Bulk density } \rho = \frac{\text{Mass of the powder}}{\text{bulk volume of the powder}} = \frac{M}{V_b}$$

Where,
ρ_b = Tapped density
M = mass of powder taken
V_b = bulk volume of powder
A given quantity of the powder is transferred to the measuring cylinder and it is tapped mechanically either manually or mechanical device till a constant volume is obtained. This volume is bulk volume (v) and it includes the true volume of the powder and void space among the powder particles.

Tapped density:
Tapped density is defined as the ratio between weight of the sample powder taken and the tapped volume.

$$\textbf{Tapped density } (\rho t) = \frac{\text{Mass of the powder}}{\text{tapped volume of the powder}} = \frac{M}{Vt}$$

Where,
ρ_t = Tapped density
M= weight of sample powder taken
$\mathbf{V_t}$= tapped volume

Method: A weight quantity of powder blend previously shaken to break any agglomerates formed was introduced into a measuring cylinder and volume was noted. The cylinder was the tapped density apparatus and allowed to fall under its own weight on to hard surface ,that provides fixed a drop of 3mm(±10%) at a nominal rate of 250 drops per minute is used. Tapping was continued until no further change in volume was noted. Carr's index

(Compressibility index):
The bulk volume and tapped volume was measured and compressibility index was calculated using the formula.

$$\textbf{Compressibility index } = 100 \times \frac{\text{Bulk volume } - \text{Tapped volume}}{\text{bulk volume}} = \frac{\mathbf{Vb - Vt}}{\mathbf{Vb}}$$

Where,
Vb = Bulk volume
Vt = Tapped volume.

Table: 2 Relationship between % Compressibility and flowability

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Sr.No	% Compressibility	Flowability
1	5-15	Poor
2	12-16	Fairly acceptable
3	18-21	Good
4	23-35	Excellent
5	33-38	Very poor
6	>40	Extremely poor

Hausners ratio:

By using following formula, the Hausners ratio can be calculated.

$$\text{Hausners ratio} = 100 \times \frac{\text{Tapped volume}}{\text{bulk density}} = \frac{\rho t}{\rho b}$$

Where,

ρ_b= Bulk density

ρ_t= Tapped density

Table: 3 Table of Hausners ratio

Sr.No	Hausners ratio	Property
1	1.00-1.11	Excellent
2	1.12-1.28	Good
3	1.19-1.24	Fair passable
4	1.25-1.34	Passable
5	1.35-1.45	Poor
6	1.46-1.54	Very poor
7	>1.55	Very very poor

Loss on drying (LOD):

Loss on drying of blend was study. This was measured by Mettler-Toledo.

EVALUATION OF POST –COMPRESSION PARAMETER: [2-3, 7-8, 10, 15, 19]

Appearance:

The tablets were visually observed for capping, chipping, and lamination.

Tablet Dimensions/ Thickness:

Thickness and diameter were measured using a calibrated vernier caliper. Tablets of each formulation were picked randomly and thickness was measured individually. Ten tablets from each type of formulation were used and average values were calculated. It is expressed in mm.

Hardness:

The resistance of tablets to shipping, breakage, under conditions of storage, transportation and handling before usage depends on its hardness. For each formulation, the hardness of 20 tablets was determined using the Monsanto hardness tester. The tablet was held along its oblong axis in between the two jaws of the tester.

At this point, reading should be zero kg/cm^2. Then constant force was applied by rotating the knob until the tablet fractured. The value at this point was noted.

Friability:

Friability is the measure of tablet strength. Roche Friabilator was used for testing the friability using the following procedure. This

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test subjects a number of tablets to the combined effect of shock abrasion by utilizing a plastic chamber which revolves at a speed of 25 rpm, dropping the tablets to a distance of 6 inches in each revolution. A sample of pre weighed 6 tablets was placed in Roche friabilator which was then operated for 100 revolutions i.e. 4 minutes. The tablets were then dusted and reweighed. A loss of less than 1 % in weight in generally considered acceptable.

Percent friability (% F) was calculated as follows

$$\textbf{Percent friability \% F} = \frac{\text{Initial weight} - \text{Final weight}}{\text{Initial weight}} \times 100$$

Weight variation test:

To find out weight variation, 20 tablets of each type of formulation were weighed individually using an electronic balance, average weight was calculated and individual tablet weight was then compared with average value to find the deviation in weight (Indian pharmacopoeia,)

Table: 4 Specifications for Tablets As Per Pharmacopoeia Of India

Specifications for tablets as per Pharmacopoeia of India		
Sr No.	**Average Weight of Tablet**	**% Deviation**
1	80 mg or less	10
2	More than 80 mg but less that 250 mg	7.5
3	250 or more	5

Drug Content Uniformity:

10 tablets from each batch were weighed accurately and powdered. Weight the quantity of powder equivalent to 100mg telmisartan, was shacked with 100ml of phosphate buffer 7.5 in 100ml of volumetric flask, and from this 10ml was pipette out and then dilute upto 100ml from this standard solution again 10ml pipette out and dilute upto 100ml volumetric flask. Resulting solution was filtered and assayed at 296nm and content of telmisartan was calculated phosphate buffer as blank.

Content uniformity was calculated using formula –

% Purity = 10 C (Au / As)

Where, C - Concentration,

Au and As - Absorbance's obtained from unknown preparation and standard Preparation respectively.

In vitro disintegration time:

The process of breakdown of a tablet into smaller particles is called as disintegration. The in-vitro disintegration time of a tablet was determined using disintegration test apparatus as per I.P. specifications.

In-Vitro dissolution Studies: [19]

For the present work in vitro dissolution studies were carried out in (phosphate buffer of PH7.5) 0.1N HCl for 30 minutes using 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±0.20C. the tablet are kept in the cylindrical basket or directly placed in medium with paddle then rotated at 100 rpm.5 ml of the sample from the dissolution medium are withdrawn at each time interval (5,10,15&30

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minutes) and 5 ml fresh medium was replaced each time. The samples were filtered and from the filtrate 1 ml was taken and dilute to 10 ml. These samples were analyzed spectophotometrically 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) .the in vitro dissolution kinetic parameters, dissolution rate constants correlation coefficient and dissolution efficacy were calculated.

Evaluation Stability Study: [16]

In any rational design and evaluation of dosage forms for drugs, the stability of the active component must be a major criterion in determining their acceptance or rejection.

Stability of a drug can be defined as the time from the date of manufacture and the packaging of the formulation, until its chemical or biological activity is not less than a predetermined level of labeled potency and its physical characteristics have not changed appreciably or deleteriously.

Objective of the Study:

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.

Generally, the observation of the rate at which the product degrades under normal room temperature requires a long time. To avoid this undesirable delay, the principles of accelerated stability studies are adopted.

The International Conference on Harmonization (ICH) Guidelines titled “stability testing of New Drug substance and products” (QIA) describes the stability test requirements for drug registration applications in the European Union, Japan and the United States of America.

CONCLUSION

This is new enhanced oral product arising within this market there is a clear opportunity for new enhanced oral product arising with this larger market segment. 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 dosages format the immediate release (IR) pharmaceutical forms has been developed which offers the combined advantages of ease of dosing and convince of dosing. These tablets are designed to release the medicament with an enhanced rate. Due to the constraints of current technology as highlighted above, there is an unmet need for improved manufacturing processes for immediate release pharmaceutical strong to allow good packing and manufacturing by using above different superdisintegrant and technology.

To fulfill these medical needs, formulation have devoted considerable efforts to developing a novel types of tablet dosages for oral a administration, one that disintegrant and dissolve rapidly with enhanced dissolution. an extension of market exclusivity, which can be provide by immediate release dosage form leads to increase revenue, while also targeting underserved and under –treated patent population.

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