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ADVANCEMENT IN IMMEDIATE RELEASE TABLETING: A REVIEW

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ABSTRACT
Tablet is the utmost 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 alternate oral dosage forms. There are novel types of dosage forms that act very rapidly after administration. The basic approach used in development tablets is the use of super-disintegrants likeCroscarmellose, Primogel, Kollidon CL etc. which provide immediate disintegration of tablet after administration. The current development in immediate release tablets such as Novel granulation technologies, electrostatic dry powder coating process, Novel Hole Technology in Fast Dissolving Tablets, Hot-Melt Extrusion and Injection Molding also provides an opportunity for a line extension in the market place.

KEYWORDS: Immediate Release formulation; Super-Disintegrant; Granulation; Compression.

INTRODUCTION
Oral administration is the most popular route for systemic effects due to its ease of ingestion, pain, avoidance, adaptability, less expensive to manufacture, high-precision dosing, manufacturing efficiency and most importantly Patient compliancemake tablets the solid dosage form of choice.Also, solid oral delivery systems do not require sterile conditions and are therefore, less affluent to manufacture. Patient compliance, high accuracy dosing, and manufacturing efficiency make tablets the solid dosage form of choice. Excipients and equipment's choices will be significantly affected should solid dosage form technologies change in response to the unparalleled shifts in the drug discovery such as genomics. Injections generally are not favoured 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 mostly chemical entities with low molecular weights.

Tablet provides high precision dosing. In most of the cases immediate on set of action is required as compare to conventional therapy. To achieve the rapid onset of action and eliminate the drawbacks of conventional therapy immediate release dosage form is nowadays popular oral dosage form. Many patients require quick onset of action in particular therapeutic condition and consequently immediate release of medicament is required. Enhancement of dissolution can be done by using super disintegrants. Super-disintegrants, disintegrate the tablet quickly which enhances the dissolution rate of the drug.

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 diluent or carrier, which diluent or carrier does not prolong, to an appreciable extent, the rate of drug release and/or absorption.

Immediate release solid oral dosage forms are classified as moreover having rapid or slow dissolution rates. Immediate release dosage forms are those for which ≥85% of labelled amount dissolves within 30 min.,simple disintegration or erosion stageis the only barrier to drug releasefor immediate release tablets, which is generally accomplished in less than one hour. To enhance dissolution and hence bioavailability of any drug from immediate. For immediate release tablets, disintegration is one of the important process. Few Super-disintegrant are available commercially as Croscarmellose sodium, Crospovidone and Sodium Starch Glycolate.[1]

Salient Features of Immediate Release Drug Delivery System:[2]

- Drug should possess extended biological half-life for immediate release drug delivery
- The drug is released rapidly and completely in one shot
- Poor solubility of the drug and need the immediate action of drug
- Lower clearance and lower elimination half -life
- High bioavailability expected with immediate release dosage form
- Rapid drug therapy intervention is probable
- But main criterion for immediate release dosage form is poor solubility of the drug and need the immediate action of drug to treat undesirable defect or disease

Measures for Immediate Release Drug Delivery System[3,4]

Immediate release dosage form should in the case of solid dosage it should dissolve or disintegrate in the stomach within a short period.

- In the case of liquid dosage form it should be companionable with taste masking.
- Be transferrable without fragility concern.
- Have a pleasing mouth feel.
- 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.

Difficulties with Oral Dosage Form:[5]

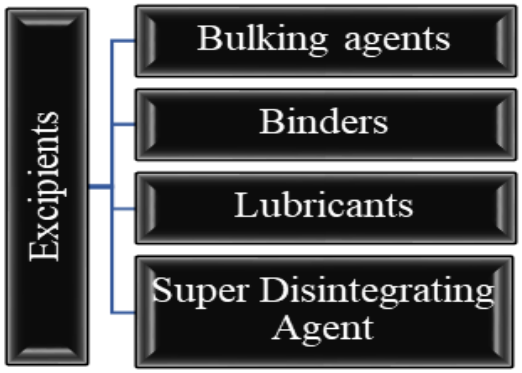
- Patient may suffer from tremors consequently they have difficulty to take tablet, powder and liquids. In dysphasia physical obstacles and adherence to an oesophagus may cause gastrointestinal ulceration.
- Swallowing of solid dosage forms like tablet and capsules and produce difficulty for young adult of partial development of muscular and nervous system and elderly patients suffer from dysphasia.

Advantages of Immediate Release Drug Delivery System:[6,7]

- Improved compliance/added convenience
- Improved stability
- Suitable for controlled/sustained release actives
- Allows high drug loading
- Ability to provide advantages of liquid medication in the form of solid preparation.
- Adaptable and amenable to existing processing and packaging machinery
- Cost- effective
- More flexibility for adjusting the dose
- It can be prepared with minimum dose of drug
- There is no dose dumping problem

Excipients Used in Immediate Release Tablets:[8-15]

Excipients equilibrium the properties of the actives in Immediate release dosage forms. This demands a thorough understanding of the properties of these excipients to prevent interaction with the actives. Determining the cost of these ingredients is additional 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 efficiency.



Bulking agents.

Bulking agents are significant used in the formulation of fast-dissolving tablets. The material contributes essentials of a diluents, filler and cost reducer. Bulking agents enhance the textural characteristics that in turn improve the disintegration in the mouth, other than; adding bulk also lessen the concentration of the active in the composition. The suggested bulking agents for this delivery system should be more sugar-based, e.g. mannitol, polydextrose, lactitol, DCL (direct compressible lactose) and starch for higher aqueous solubility and good sensory perception. Bulking agents are added in the range of 10 percent to about 90 percent by weight of the final composition.

Binders

Binders are the excipients that holds powders together to form granules. They are the adhesives that are added to tablet formulations to provide the cohesiveness required for that bonding together of the granules under compaction to form a tablet. The quantity used and the method of application must be carefully controlled, since the tablet must remain intact when swallowed and then release its medicament.

Lubricants

Lubricants, though not vital excipients, can further assist in making these tablets more palatable after they disintegrate in the mouth. Lubricants remove grittiness and assist in the drug transport mechanism from the mouth down into the stomach. e.g. Magnesium stearate, Stearic acid.

Super disintegrants
A disintegrant is an Excipients, which is included to a tablet or capsule blend to support in the breakup of the compacted mass when it is put into a fluid environment e.g. cross carmallose sodium, sodium starch glycolate andCross-linked Povidone.

The use of super disintegrants for the preparation of immediate release tablets are highly effective and commercially feasible. These super disintegrants accelerate disintegration of tablets by quality of their ability to absorb a large amount of water when exposed to an aqueous environment. The absorption of water results in breaking of tablets and therefore faster disintegration. This disintegration is reported to have adirect effect on dissolution characteristics as well.

Advantages of Super disintegrants
- Effective in lower concentrations
- Less effect on compressibility and flow ability
- More effective intragranularly

Mechanism of Disintegration[16]
- capillary action (Wicking)
- Swelling
- Due to deformation
- Due to release of gases

1. Sodium Starch Glycolate (Explotab, Primogel) utilized in concentration of 2-8% & optimum is 4%.

Mechanism of Action: Swells 7-12 folds in < 30 seconds. Quick and extensive swelling with minimal gelling.

2. Cross-linked Povidone (crosspovidone, Kollidone, Crospovidon-M, Polyplasodone) used in concentration of 2-5% of weight of tablet. Completely insoluble in water.Killodon are available as Kollidon CL, Kollidon CL-F, Kollidon CL-M and Kollidon CL-SF in market. Swelling properties paired with particle size distribution make the fine Kollidon CL-grades work efficiently in fast disintegrating formulations.

Mechanism of Action: Swells very little and returns to original size after compression but act by capillary 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. Quickly swells in water. Grades LH-11 and LH-21 shows the greatest degree of swelling. Many grades can also provide some binding properties while retaining disintegration capacity. It used in concentration 1-5%.

4. Cross linked carboxy methyl cellulose sodium (i.e. Ac-Di-sol, Croscarmellose sodium, Nymeee ZSX, Primellose, Solutab, Vivasol): Effective Concentrations is 1-3% for Direct Compression and 2-4% for Wet Granulation.

Mechanism of Action: Swells 4-8 folds in < 10 seconds. Swelling and wicking due to fibrous structure, swelling with minimal gelling.

Technology for Immediate Release Tablets[17-20]
1. Tablet molding technique
2. Direct compression technique
3. Wet Granulation technique
4. Mass extrusion technique

Numerous Technologies are available to manufacture immediate release tablets. The most common preparation methods are moulding technique, Direct compression technique, Granulation technique and mass extrusion technique.

Tablet molding technique
Water-soluble ingredients are used in tablet molding technique which facilitate tablet to disintegrate and dissolve quickly. A hydro alcoholic solvent use to moisten powder blend and is molded in to tablet using compression pressure lesser than used in conventional tablets. The solvent is then removed by air-drying. Mechanical strength and poor taste masking are two problems commonly encounteredin this technique.

Mass-Extrusion
Here softening of active blend done with solvent mixture of water-soluble polyethylene glycol and methanol and subsequent exclusion of softened mass through the extruder or syringe to get a cylinder of the product into even segments using heated blade to form tablets. In case of bitter drug granules can be coated with the help of dried cylinder to achieve taste masking.

Direct Compression Method
In this method, tablets are compressed directly from the mixture of the drug and excipients without any preliminary treatment.Sift the material through #30 mesh for breakdown of lumps leads to uniform particle size. If material not passed through #30 than use #18 mesh.The mixture to be compressed must have acceptable 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.

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

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

Step 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 corn-starch, natural gums such as acacia, cellulose derivatives such as methyl cellulose, gelatine, 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.

Recent Development in Immediate Release Tablets

Miniaturized approach for excipient selection

The miniaturized Approach is high-throughput stage to understand the impact the influence of Excipients on the performance of oral solid dosage forms during early drug advancements. For the productive manufacturing of tablets, different Excipients such as binders, diluents, disintegrants, and lubricants are required. Despite the fact that Excipients are considered as inactive ingredients and are added to enhance the functionality of the dosage forms, they may have harmful impact on the performance of the dosage forms at different stages during manufacturing, storage and/or dissolution. This may be attributed to different properties of Excipients, for e.g. water-sorbing potential, phase transformation behaviour, hydrophobicity, solubility, microenvironment pH, crystallinity and chemical incompatibility with Active Pharmaceutical Ingredient (API). Thus, it is essential to investigate the effect of Excipients on the performance of oral solid dosage forms. A well-designed Excipients screening study during early advancement can help selecting appropriate Excipients that enhance the usefulness of the API. Also, it can help in the elimination of Excipients having harmful impact on the performance of API. This approach can be used for Excipients selection and for early-stage activity testing of active pharmaceutical ingredient intended for oral solid dosage form. Unexpectedly, one of the significant difficulties during early drug development is negligible accessibility of candidate drug compounds limiting the possible batch sizes and the number of studies that can be performed. Consequently, it is essential to create methods that empower accomplishing the data about the candidate drug with minimal use of resources. The current study introduces a miniaturized approach for the combined examination of the impact of the Excipients and processing-induced stress (wet granulation and compression) on the activity of oral solid dosage forms.[21]

Novel granulation technologies

The current technologies utilized for granulation contain steam granulation; Moisture Activated Dry Granulation (MADG), Moist Granulation Technique (MGT), Thermal Adhesion Granulation Process (TAGP) and foam granulation etc. have their own advantages and overcome the disadvantages of conventional granulation process for e.g. dust generation or harmful impact of heat as drying step.

Pneumatic Dry Granulation (PDG)

This is a new drug method for automatic or semi-automatic preparation of granules. It modifies the drug load along with disintegration time and tablet hardness. The PDG Technology enables preparation of porous granules having brilliant compressibility and flow ability characteristics. The pneumatic dry granulation process is fit for granulating virtually any pharmaceutical solid dosage ingredient. PDG Technology has been utilized with prevalent results in advancement of tablets having fast release, controlled release along with measured-dose, and orally disintegrating tablets. The technology can be utilizing for practically any solid dosage pharmaceutical product.

PDG technology can achieve:

- High drug loading, even with difficult APIs and combinations
- Taste masking
- Excellent stability

Nowadays, wet granulation is the most usually used. This process can granulate any pharmaceutical solid dosage ingredient. This technology is utilized for the development of tablets with quick and controlled-release along-with fixed dose and orally disintegrating tablets. PDG has replaced wet granulation technique.

Freeze Granulation Technology (FGT)

This system has been received by Swedish Ceramic Institute (SCI) which empowers protection of the homogeneity from suspension to dry granules. A powder suspension is sprayed into fluid nitrogen, the granules are frozen promptly. In a subsequent freeze-drying the granules are dried by utilizing sublimation of the ice without any segregation effects as in case of conventional drying in air. The succeeding granules will be spherical and free flowing with ideal consistency. This procedure helps in easy crushing to homogeneous and dense powder compacts in preparing operation.

Foamed Binder Technologies (FBT)
FBT from the Dow Chemical company helps in accomplishing faster, simpler and more secure wet granulation. This method utilizes METHOCEL polymers and greatly enhanced binder distribution in the formulation blend and yields a notable array of processing advantages. It helps in decreasing water prerequisites, enhanced reproducibility. It helps in eliminating spray nozzles and their numerous variables in granulation preparing equipment.

One can without much of a stretch use it with recognizable high shear, low shear, or fluid bed granulation equipment, in both laboratory and production scale backgrounds. Our evaluation also demonstrates it yields well known metrics for particle size distributions, solid dose physical properties and dissolution profiles.

It gives advantage of tremendous increase in the liquid surface area and volume of polymeric binder foams to enhance the distribution of the water or binder system throughout the powder bed of pharmaceutical formulation of solid dose.

Melt Granulation Technology (MGT)
This is method with the assistance of which granules are obtained through the incorporation of either a molten binder or a solid binder which melts during the process. This technique is also called melt agglomeration and thermoplastic granulation.

Steam Granulation Technology (SGT)
This method is a modification of wet granulation. We utilize steam as binder rather than water. Pure steam is a transparent gas. At a standard temperature and pressure (mixed with air, but in equilibrium with liquid water) it involves around 1600 times volume of an equal mass of fluid water. The granulation of particles includes the injection of appropriate amount of fluid as steam. This steam injection strategy utilizes the utilization of steam at 150 ℃ and have a tendency to deliver.

Moisture Activated by Dry Granulation (MADG)
This technology is also called "Single pot granulation".

- Moisture is utilizing in order to activate the granules formation but the granule drying process is not needed due to moisture absorbing material such as microcrystalline cellulose.
- This technique comprises of two stages, wet agglomeration of powder blend followed by moisture absorption stages.
- 1-4% water is added first keeping in attention the end goal to agglomerate the blend of API, a binder and excipients. Moisture absorbing material such as MCC alongside potato starch is added to absorb the excess amount of moisture.
- After the lubricant has been blended, the blend obtained can be compressed directly into the tablets. Hence, this process offers few advantages of wet granulation.

Advantages

- Very little granulating fluid is used.
- Drying time is reduced and the granules created have good flow ability.
- Single production equipment such as high shear granulator is used.
- No equipment changes and lower tablet capping.
- No over and under granulation.
- It is applicable for building up a controlled released formulation.

Thermal Adhesion Granulation Process (TAGP)
It is useful in manufacturing tableting formulations. This procedure is performed under low moisture content or low content of pharmaceutically acceptable solvent by subjecting a blend including one or more diluents and active ingredients; a binder; alternatively, a disintegrant to warm at a temperature ranging from 30℃-1300℃ in a closed system under blending by tumble rotation until the formation of the granules occurs. It utilizes less water than the wet granulation approach. It gives granules with very good flow properties and binding capacity to form tablets which have low friability with adequate hardness and have a high loading of active substances whose tableting is poor. It additionally minimizes the generation of dust particles during the preparation. This method serves to contain fine-powder active ingredients whose spread or loss from system is not required because of their cost or biological activity.

TOPO (TOPO Granulator) Technology
Hermes Pharma has built up a unique technology for doing single pot granulation. This procedure requires a little amount of fluid to begin the chain reaction. Pure water or water-ethanol blend are utilized.

TOPO Technology produces granules for tablets which in any event contains one solid crystalline, an organic acid and one alkaline or alkaline earth metal carbonate that reacts with the organic acid in aqueous solution to produce carbon dioxide. Therefore, there are no solvent remains in the final products; granules have excellent hardness and stability. TOPO Granulator was used for creating for effervescent tablets following TOPO vacuum to prevent uncontrolled chain reaction.

Continuous Flow Technology
This technology does not require any liquid to begin the chain reaction. For this situation granulation is done in slanted drum into which powder is fed at one end and granulate is removed at the other. The procedure produces granule with surface ensured by inactive component that do not harm the sensitive API. This technology can formulate upto12 tons of granules every day.

Advantages

- Sensitive APIs are protected.
- Granules and effervescent become less sensitive to humidity and high temperature.
- Granules form significantly stable products.
- No solvent remains in the finished products.

Granulex technology

This technique performs both coating and powder layering process. Different coating and powder layers demonstrate the precision and control of a granulex rotor process, including the production of non-pareil.

Key-Features: Unique, Efficient granulation forms. Granules delivered are thick and spherical in shape. One Pot Processing: It has the capacity of drying the product in the same handling compartment. This strategy in blend with 12 bar development gives a true one pot system which is ideal for manufacturing of highly potent and expensive pharmaceutical compounds.[22,23]

Hot-melt extrusion and injection molding for continuous manufacturing of immediate-release tablets

In the most recent 10 years, the interest for the potential use of Continuous Manufacturing (CM) to the pharmaceutical field has been growing. 3-6cm comprises in creating/preparing, without interference, materials generally maintained in movement and experiencing chemical reactions or mechanical/heating treatments. As indicated by the USFDA, continuous processing has the potential for enhancing product quality, and the industry is encouraged to openly consider a shift in this direction. Advantages related to CM are evident. It could lessen the time and expenses of development simply by avoiding the moving of materials among facilities, constraining the put away amount of dangerous chemicals thus enhancing sustainability, overcoming the requirement for stopping, reconfiguration and testing between batches as well as that for scaling up. A model Immediate-Release (IR) tablet was accomplished by extruding and injecting an essential thermoplastic formulation, made up of an in situ synthesized model drug and Polyethylene Glycol (PEG), into appropriately formed mold. Hot-processing methods, such as Hot-Melt Extrusion (HME) and Injection Molding (IM), would particularly be suitable for filling the requirements of CM. HME has successfully been applied to improve the dissolution rate/bioavailability of drugs by advancing the formation of solid dispersions with thermoplastic carriers, and, again, a couple of products reached the marketplace. With respect to IR dosage forms, starch-based injection-molded shells were proposed as a different option to dip-moldedgelatin capsules. Furthermore, powders or granules got from milling of extruded dispersions may be compressed to give IR tablets. The utilization of these processing methods would also result in the possibility of carrying out solventfree processes, overcoming blending and/or compaction problems, patenting the obtained products and improving the relevant adaptability as far as size/shape.[24]

Novel hole technology

The fundamental target of this technology is to design and development of Fast dissolving tablets by novel hole technology. It is a novel way to deal with decreasing the disintegration time and build the patient compliance. By utilizing this technology total surface area of the tablet increment because of hole formation. Quick breaking of the tablet happens because of the liquid goes into the hole formed in the tablet. A few technologies were developed to improve the disintegration time but the tablets manufactured by hole technology have expanded surface area due to formation of hole and expanded pore structure. The principle included in hole technology is sublimation. Highly volatile ingredients like ammonium bicarbonate, ammonium carbonate, benzoic acid, camphor, naphthalene, urea, urethane and phthalic anhydride might be compressed along with different excipients into a tablet. This added volatile material is then removed by sublimation leaving behind a highly porous matrix. Tablets made by this technology have reported to usually disintegrate in 10-20 seconds. The tablets manufactured with hole technology demonstrated all the parameters like hardness, friability, weight variation inside the limits.[25]

A novel electrostatic dry powder coating process

Polymer film coat is mostly applied in pharmaceutical dosage forms to achieve aesthetic quality, taste masking, enhancement of stability, and modification of drug release. The coating procedure is generally based on the dissolution or dispersion of polymeric materials in organic or aqueous solvents. The use of organic solvent experiences the toxicological, environmental, expense and safety-related issues. These disadvantages have been solved by the introduction of aqueous-based coating technology. However, aqueous film coating needs a slower drying process and high energy input because of the high heat of evaporating water (539.4cal/ g). Different issues experienced with aqueous film coating are lower solid content in the coating solution and risk of microbial contamination. The presence of water during the coating process and residual moisture in the film can influence stability of certain water sensitive drugs. Thus, eliminating solvents in the pharmaceutical film coating is thought to be a powerful approach to lessen production cost, improve process efficiency and enhance product quality. An electrostatic dry powder coating process for pharmaceutical solid dosage forms was produced for the first time by electrostatic dry powder coating in a pan coater system. Two immediate release coating compositions with Opadry AMB and Eudragit EPO were effectively applied using this process. The use of fluid plasticizer was followed by spraying charged coating particles utilizing an electrostatic charging gun to improve the uniform deposition on tablet surface. The electrostatic powder coating technique can produce smooth and uniform coating film and has been exhibited

as a promising different option to conventional aqueous-based coating process.[26]

A flexible-dose dispenser for immediate 3D printed tablet

Personalized medicine provides patients with a superior treatment that thinks about their Pharmacogenomics, anatomical and physiological particulars. One major clinical part of personalised medicine is individualizing the dose to suit an individual patient's requirement. It is of significant importance to change standardized dose tablet regimes with a dynamic-dose dispenser, which gives fast and effective assembling to individual patient's needs. For a tablet preparation technique that meets the demands of personalised medicine, a safe and effectively adaptable dispensing station must be made. The station ought to be worked through a basic client interface with small operation preparing required and can be associated with the more extensive human service system. Clearly, such criteria cannot be satisfied by traditional tableting methods. The use of 3D printing as an adaptable option strategy to traditional tableting techniques was first created using powder-based 3D printing technologies. Fused Deposition Modelling (FDM) is a broadly utilized and reasonable bench top 3D printing technique. The capability of FDM-based 3D printers to consolidate drug molecules has already been investigated utilizing economically accessible PVA filaments. The capability of this printing technology to give a mini-dispensing dose controlling station by controlling the volume of the printed design through an order from computer software. Nevertheless, past endeavours with FDM-based 3D printing shows a few limitations, for example, limited drug loading, the utilization of non-pharmaceutical grade ingredients, high temperature and fundamental tablet designs.[27]

Evaluation of Precompression parameters /Blend[28]

The prepared blend is evaluated by following tests;

- **Angle of repose**
- **Tapped density**
- **Bulk density**
- **Carr's index**
- **Hauser's ratio**

Angle of repose

Flow properties of the powder, resistance to particle movement can be judged from the angle of repose. Flow properties of the powder mixture are the determinant of the uniformity of the weight and thus content of the tablets. 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 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.

$$\tan\emptyset = \frac{h}{r}$$

Where,

h and r are the height and radius of the powder Pile.

Flow property also find out using flodex apparatus.

Bulk density

Apparent bulk density was determined by pouring a weighed quantity of blend into graduated cylinder and measuring the volume and weight.

$$Bulk\ Density = \frac{Weight\ of\ Powder}{Volume\ of\ Powder}$$

Tapped Density

It was determined by placing a graduated cylinder, containing a known mass of drug-excipients blend. The cylinder was allowed to fall under its own weight onto a hard surface from the height of 10cm at 2- second intervals. The tapping was continued until no further change in volume was noted.

$$Tapped\ Density = \frac{Weight\ of\ Powder}{Tapped\ volume}$$

Nowadays, Electro Lab forms tapped density apparatus with type I and II apparatus. Number of tapping was follows as 10, 500, 1250 and after 1250 tapping volume change is more than one than again 1250 tapping was performed.

Carr's index

Compressibility is the ability of powder to decrease in volume under pressure using bulk density and tapped density the percentage compressibility of powder was determined, which is given as Carr's compressibility index. It is indirectly related to the relative flow rate. Carr's compressibility index was determined by the given formula.

$$\text{Carr's Index} = \frac{Bulk\ Volume - Tapped\ Volume}{Bulk\ Volume} \times 100$$

Hausner's ratio

Hausner's ratio indicates the flow properties of powder and measured by the ratio of tapped density to bulk density. Hausner's ratio was determined by the given formula:

$$\text{Hausner's Ratio} = \frac{Tapped\ Density}{Bulk\ Density}$$

Evaluation of Post compression parameter / Tablets.[29]

The tablets are subjected to the following quality control tests which are classified into two categories;

1. **Official Quality Control Tests (**Mentioned in Pharmacopoeia**)**
2. **Unofficial Quality control tests (**Not mentioned in Pharmacopoeia**)**

Official Quality Control Tests

1. Weight Variation

Weigh individually 20 units selected at random or, for singledose preparations in individual containers, the contents of 20 units, and calculate the average weight. Not more thantwo ofthe individual weights deviate from the average weight by more than the percentage shown in the table and none deviates by more than twice that percentage.

Average weight	Percentage deviation
80 mg or less	± 10 %
More than 80 mg but less than 250 mg	± 7.5 %
250 mg or more	± 5 %

2. Content Uniformity

The test for uniformity of content of single-dose preparations is based on the assay of the individual contents of active substance(s) of a number of single-dose units to determine whether the individual contents are within limits set with reference to the average content of the sample.

Method: Determine the content of active ingredient(s) in each of 10 dosage units taken at random using the method given in the monograph or by any other suitable analytical method.

Acceptance limits: The preparation complies with the test if each individual content is 85 to 115 per cent of the average content. The preparation fails to comply with the test if more than one individual content is outside these limits or if one individual content is outside the limits of 75 to 125 per cent of the average content. If one individual content is outside the limits of 85 to 115 per cent of the average content but within the limits of 75 to 125 per cent, repeat the determination using another 20 dosage units. The preparation complies with the test if not more than one of the individual contents of the total sample of 30 dosage units is outside 85 to 115 per cent of the average content and none is outside the limits of 75 to 125 per cent of the average content.

3. Dissolution Test

Place the stated volume of the Dissolution Medium (±1%) in the vessel of the specified apparatus given in the individual monograph, assemble the apparatus, equilibrate the Dissolution Medium to 37 ± 0.5°, and remove the thermometer. Place 1 dosage unit in the apparatus, taking care to exclude air bubbles from the surface of the dosage unit, and immediately operate the apparatus at the specified rate given in the individual monograph. Within the time interval specified, or at each of the times stated, withdraw a specimen from a zone midway between the surface of the Dissolution Medium and the top of the rotating basket or blade, not less than 1 cm from the vessel wall. [NOTE— Where multiple sampling times are specified, replace the aliquots withdrawn for analysis with equal volumes of fresh Dissolution Medium at 37° or, where it can be shown that replacement of the medium is not necessary, correct for the volume change in the calculation. Keep the vessel covered for the duration of the test, and verify the temperature of the mixture under test at suitable times]. Perform the analysis as directed in the individual monograph using a suitable assay method.Repeat the test with additional dosage form units.

4. Disintegration test

Disintegration time is very important for immediate release tablets as it assists swallowing and also plays a role in increasing drug absorption, thus promoting bioavailability.

Method: Unless otherwise stated in the individual monograph, introduce one tablet or capsule int6 each tube and, if directed in the appropriate general monograph, add a disc to each tube. Suspend the assembly in the beaker containing the specified liquid and operate the apparatus for the specified time. Remove the assembly from the liquid. The tablets or capsules pass the test if all of them have disintegrated. If 1 or 2 tablets or capsules fail to disintegrate, repeat the test on 12 additional tablets or capsules; not less than 16 of the totals of 18 tablets or capsules tested disintegrate. If the tablets or capsules adhere to the disc and the preparation under examination fails to comply, repeat the test omitting the disc. The preparation complies with the test if all the tablets or capsules in the repeat test disintegrate.

Unofficial Quality control tests

1. Friability

This test is applicable to compressed tablets and is intended to determine the physical strength of tablets.

Apparatus: Friability test Apparatus

Method: 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 0.65g take a sample of 10 whole tablets. Dedust the tablets carefully and weigh accurately the required number of tablets. Place the tablets in the drum and rotate it 100 times. Remove the tablets, remove any loose dust from them and weigh them accurately. The test is run only once unless the results are difficult to interpret or if the weight loss is greater than the targeted value, in which case, the test is repeated twice and the mean of the three tests is determined. A maximum loss of weight (from a single test or from the mean of the three tests) not greater than 1.0 per cent is acceptable for most tablets.

2. Hardness

Hardness (diametric crushing strength) is a force required to break a tablet across the diameter. The hardness of a tablet is an indication of its strength. The tablet should be stable to mechanical stress during handling and transportation. The degree of hardness varies with the different manufactures and with the different types of tablets. Hardness of tablet was measured by Monsanto hardness tester. Hardness of tablet were representing as mean ± SD. For immediate release tablet hardness was controlled around 90 N.

3. Thickness

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

CONCLUSION

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 enhanced 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.Most of the patients need rapid therapeutic action of drug, resulting in poor compliance with conventional drug therapy which leads to minimize therapy effectiveness. Immediate release tablets are designed to release the medicaments with an enhanced rate. A new approach i.e. immediate release has been developed which offers the combined advantages of ease of dosing and convenience of dosing. To fulfil these medical requirements, formulators have enthusiastic considerable effort to developing a novel type of tablet dosage form prepared by novel techniques such as Novel granulation technologies, electrostatic dry powder coating process, Novel Hole Technology in Fast Dissolving Tablets, Hot-Melt Extrusion and Injection Molding for Unceasing Manufacturing of Immediate-Release Tablets for oral administration, one that disintegrates and dissolves rapidly with improve dissolution and also for selection of Excipients novel Miniaturized approach is used.

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