WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES
SJIF Impact Factor 7.421
Volume 8, Issue 4, 590-603 Review Article ISSN 2278 – 4357

A REVIEW ON FORMULATION TECHNIQUES AND EVALUATION FOR IMMEDIATE RELEASE TABLET

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Article Received on
07 Feb. 2019,
Revised on 28 Feb. 2019,
Accepted on 22 March 2019
DOI: 10.20959/wjpps20194-13481

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ABSTRACT

In recent decades, a variety of pharmaceutical research has been conducted to develop new dosage forms assume quality of life, most of these efforts have been focused on ease of medication. In present research, Pharmaceutical products designed for oral deliverydosage form. Recently Immediate release tablet is the most popular among all delivery system existing today because of its convenience of self-administration, compactness and easy manufacturing and Many patients want to quick onset of action in particular therapeutic condition and consequently immediate release formulation is required. Immediate drug release dosage forms disintegrate rapidly after administration with enhanced rate of dissolution. For the development of immediate release dosage form the basic techniques used, as direct compression, wet granulation, etc. by using a diluents or filler & superdisintegrant, superdisintegrants like Sodium starch glycolate carboxymethylcellulose (Croscarmellose), Cross linked Polyvinylpyrrolidone or crospovidone (Polyplasdone) etc. these superdisintegrants are improved disintegration of tablet after adminstration in stomach. Development of immediate release dosage form is a golden tool for expanding marketplace, they are allows for manufacturer to extend market exclusivity, extending product life cycles and generating opportunity.

INTRODUCTION

Recently immediate release tablets have started gaining popularity and acceptance as a drug delivery system, mainly because they are easy to administer, give quick onset of action is economical and lead to better patient compliance.

In that present study the novel drug delivery systems are developed for expanding indications, extending product life cycles and generating opportunities. Among all the different routes of administration, Oral administration is the most popular route for systemic effects due to its ease of ingestion, pain, avoidance, versatility and most importantly patient compliance.[1] Immediate release dosage form allows a manufacturer to extend market exclusivity, while Many patients want to quick onset of action in particular therapeutic condition and consequently immediate release formulation is required. It is estimated that 50% of the population is affected by this problem, which results in a high incidence of ineffective therapy.

IMMEDIATE RELEASE DOSAGE FORM

Immediate release oral dosage forms, i.e., tablets and capsules, are most widely used drug delivery systems available. Immediate release formulation are those which disintegrate rapidly and get dissolved to release the medicaments. Immediate release dosage form may be provided by an appropriate pharmaceutically acceptable diluents or fillers, like Dibasic calcium phosphate, pharmatose, avicel etc and disintegrants like Cross linked carboxymelhylcellulose (Croscarmelose), Sodium starch glycolate (Primogel, Explotab), Polyvinylpyrrolidone(Povidone) etc. which provide immediate disintegration of tablet after administration.[1,2] These products are designed to disintegrate in the stomach followed by their dissolution in the fluids of the gastrointestinal Tract. Dissolution of the drug substance, under physiological conditions, is essential for its systemic absorption.[3,10]

Biopharmaceutic Consideration

Pharmacokinetics

In this consideration, study has done on absorption, distribution, metabolism and excretion.[1,3,6]

Pharmacodynamic[1,3,6,8]

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 α-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. 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, anti-hypertensive etc. for immediate release dosage forms. The combination choice depends on disease state of the patient.

Drug selection criteria for Immediate release tablet[1,3,6]

1. Drug should have a pleasing mouth feel.
2. It should exhibit low sensitivity to environmental condition as humidity and temperature.
3. It should be manufactured using conventional processing and packaging equipment at low cost.
4. It should rapidly dissolve and absorbed from stomach.
5. It should not leave minimal or no residue in the mouth after oral administration.

Advantages of immediate release drug delivery system.

An immediate release pharmaceutical preparation offers

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

General Excipients Used In Immediate Release Tablets[1,5,7,10,12,13,16]

They must be free of any unacceptable microbiological load. They must be color compatible, should not change shade of color in the formulation. If product is classified as food, the diluents and other excipients must be approved food additives. They must not have an adverse effect on the bioavailability of the products. They must be non-toxic with no pharmacological activity and acceptable to the regulatory agencies in the countries where the product is to be marketed. Cost effective. They must be physiologically inert. They must be physically and chemically stable by themselves and in combination with other drugs and tablet components.

Role	Function	Examples	Concentration
Diluents	Fillers used to make up the volume of bulk of tablet.	Avicel 101 and 102, Dibasic calcium phosphate etc	20-90%
Binders	Provides cohesive strength to powdered materials.	Hydroxy propyl methyl cellulose, acacia, Pvpk30, cellulose derivative etc.	5-15%
Lubricants	Used to reduce the friction between die wall and tablet, prevent adhesion of tablet to dies and punches. Helps in easy ejection of tablets from die cavity	Stearic acid, talc, magnesium stearate, etc.	0.25-5.0%
Glidants	Helps in free flowing of granules from hopper to die cavity. Minimize friction between particles.	Colloidal Silicon dioxide (Aerosil) Silica derivatives etc.	0.1-1%
Anti-adherent	Prevent sticking of tablet to dies and punches.	Talc, polyethylene glycol, Castor oil, etc.	0.1-5%
Disintegrants:	Used to facilitate a breakup of the tablet.	Sodium starch glycolate, croscarmellose sodium,1 Crospovidone, polyvinyl polypyrrolidone,	0.5%-5%
Surfactants	Increase the dissolution rate.	sodium laurel sulphates, sodium taurocholic acid, lecithin	1%-10%
PH Modifiers	PH stabilizers such as acidic- retard disoolution, or Basic- enhance dissolution	Acidic- citric acid or succinic acid Basic- sodium acetate or amine.	0-10%

Mechanism of Disintegrants

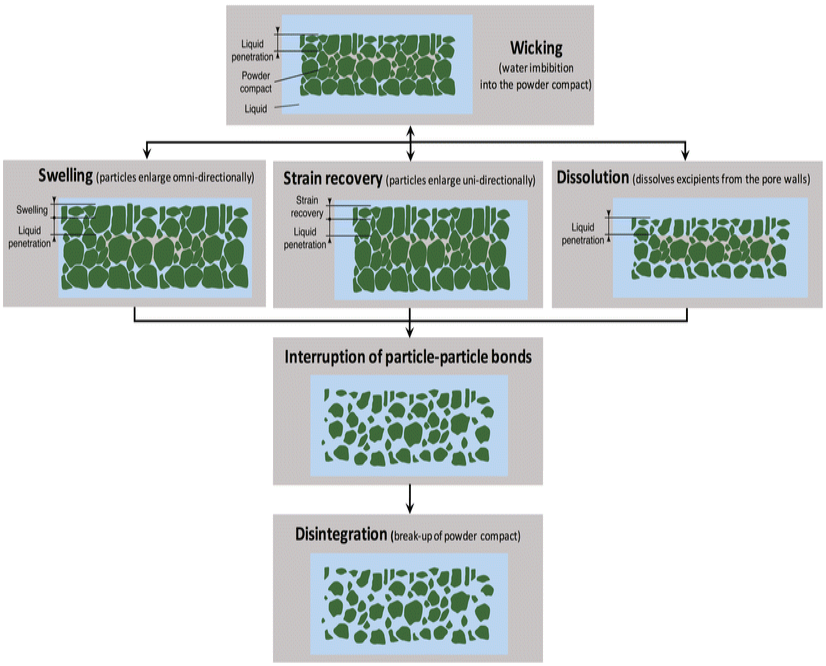


Fig: Mechanism of tablet disintegration.

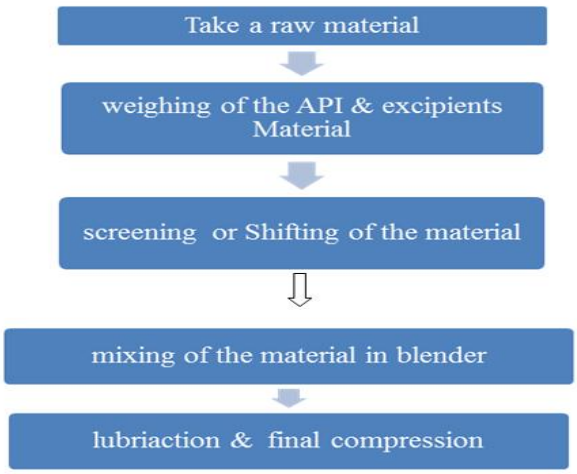
Techniques Used in the Preparation of Immediate Release Tablets

a. Tablet Molding[1]

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 molded tablets are prepared by tablet machinery or manually by forcing dampened tablet material into a mold of any shape. The formed tablet is then ejected from the mold and allowed to dry. Molded tablets have a porous structure that enhances dissolution. Two problems commonly encountered are mechanical strength and poor taste masking characteristics. Using binding agents such as sucrose, acacia or poly vinyl pyrrolidone can increase the mechanical strength of the tablet. To overcome poor taste masking characteristic 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.

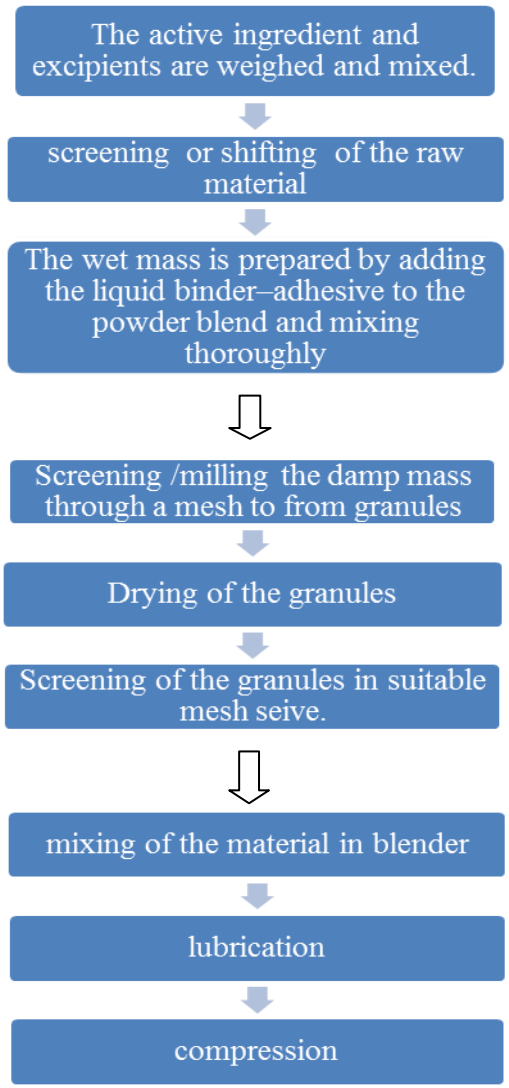
b. Direct Compression Method[5,8,15]

direct compression is a choice because it provides the shortest, most effective and fastest & safest way to produce tablet. The manufacturer can blend an API with the excipients and the lubricant, followed by compression, which makes the product easy to process. No additional processing steps are required. Moisture or heat sensitive ingredients, which would be contraindicated in wet granulation, can also be used in thios type of process. However, it does require a very critical selection of excipients in comparioson to granulation processes because the raw materials must demonstrate good flowability and compressibility for successful operation. The processing steps involved in direct compression are shown in flowchart.



Flowchart: Direct compression process.

c. Wet Granulation Method[1,8,15]



Flowchart:- Wet granulation process.

d. Mass-Extrusion[1,6,8]

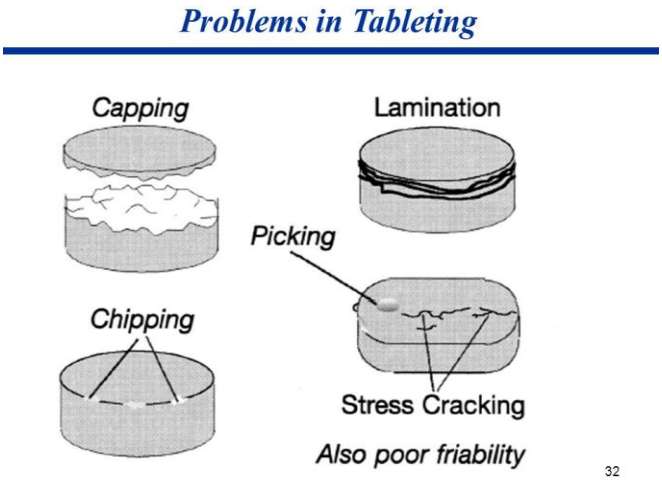
This technology involves softening the active blend using the solvent mixture of water-soluble polyethylene glycol and methanol and subsequent expulsion of softened mass through the extruder or syringe to get a cylinder of the product into even segments using heated blade to form tablets. The dried cylinder can also be used to coat granules for bitter drugs and thereby achieve taste masking.

PROBLEMS IN TABLET MANUFACTURING

Following are the defects that are found during tablet manufacturing:[1,15]

1. Weight variation
2. Capping

3. Lamination / Laminating
4. Cracking
5. Chipping
6. Sticking / Picking



EVALUATION OF IMMEDIATE RELEASE TABLETS

The blend is evaluated by following tests.[2,6,9,14]

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

1. Angle of repose

Angle of repose was determined by using funnel method. The accurately weighed blend was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of blend. The 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. 12

$$\text{Tan} = h/r$$

Where, h and r are the height and radius of the powder conc.

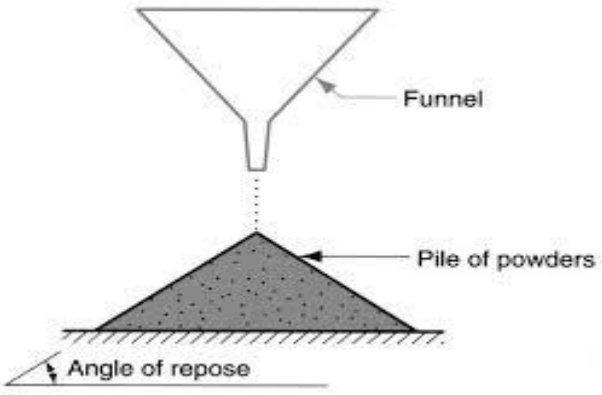


Figure: Measurement of angle of repose (Fixed Funnel method).

2. Bulk density

Bulk density was determined by pouring a weighed quantity of total mass into measuring cylinder and measuring the volume(height). Bulk density is the ratio of mass of powder to bulk volume. It was calculated in gm/cm3 by the formula.

Bulk Density (BD) = Weight of granules (m) /untapped volume of granules (v).

Here; m = weight of powder or granules (gm)

v = Bulk Volume (cm.3)

3. Tapped Density

Tapped density is ratio of mass of tablet blend to tapped volume of tablet blend. Accurately weighed amount of tablet blend poured in graduatedmeasuring cylinder and height is measured. Then cylinder was allowed to 100 tap under its own weight onto a hard surface. The tapping was continued until no further change in height was noted it was calculated in gm/cm3 by the formula.

Tapped Density (TD) = Weight of granules (m) /tapped volume of granules (v).

Here; m = weight of powder or granules (gm)

v = Tapped Volume (cm.3)

4. Compressibility Index

The Compressibility Index of the blends was determined by Carr's compressibility index.

Carr's compressibility index (%) = Compressibility is the ability of powder to decrease in volume under pressure using bulk density and tapped density the percentage compressibility of powder were 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.

Carr's Index (%) = [(TBD-LBD) X 100] / TBD

5. Hauser'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.

Hausner's Ratio =Tapped density/ Poured density

Hausner's ratio <1.25 – Good flow = 20% Carr 1.25 – Poor flow =33% Carr

6. Appearance

Acceptance of the appearance of batches of the tablet has been done based on the measurement of the following factors like size, color, shape, presence or absence of odor, taste etc.

Size and shape

The Agency recommends limiting size differences between therapeutically equivalent tablets as follows:

• If the RLD is less than 17 mm in its largest dimension, the generic product should be:

o No more than 20 percent larger than the RLD in any single dimension (the resulting single dimension of the generic should not exceed 17 mm).

o No more than 40 percent larger than the volume of the RLD.

• If the RLD is equal to or greater than 17 mm in its largest dimension, the generic product should be:

o No larger than the RLD in any single dimension.

o No larger than the volume of the RLD.

7. Weight variation

IP/BP	Limit	USP
Less than 80mg or 80mg	±10%	130mg or less
More than 80mg or less than 250mg	±7.5%	130mg to 324mg
250mg or more than 250mg	±5% ±5%	More than 324mg

Hardness

The ability of a tablet to withstand for mechanical shocks is known as hardness. Pfizer hardness tester is the instrument which is used to determine the hardness of tablet. It is expressed in kg/cm2. Take three tablets from each batch and hardness should be determined and the selection of tabled should be done randomly. Then the mean and standard devialtion values should be determined.

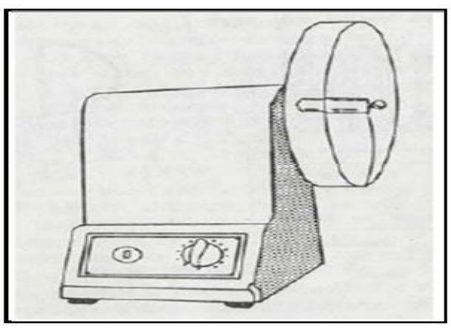
Fig: Monsanto hardness tester.

Friability

Roche friabilator is the equipment which is used for the determination of friability. It is expressed in percentage. Note down the initial weight of the tablets individually (W initial).

Tablets are placed in a plastic chamber which revolves at 25 rpm and they are subjected to fall from a height of 6 inches in the friabilator for about 100 revolutions. Then measure the weight of the tablet (Wfinal) and observe any weight difference before tablet and after the friabilator processing.

Standard says, Weight of tablet less than 650mg or 650mg,- for friability testing 6. 5gm tablets taken, &Weight of tablet more than 650mg - to take a 10 tablets for testing.



Limits: loss in weight less than 0.5 to 1% of the initial weight of the tablet should be considered as acceptable limits.

Percentage of friability is calculated as:

$$F=\{(W\ initial)-(W\ final)/(W\ initial)\}\times 100.$$

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.

Disintegration test

The USP device to disintegration was six glass tubes that are "6 long, open at the top, and held against mesh1 screen at the bottom end of the basket rack assembly. One tablet is placed in each tube and the basket rack is filled in 1 liter beaker of distilled water at 37± 2 o 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. The test measures the time required for a product to disintegrate and de-aggregate into multiparticulate system in a given medium,
Standard time of immediate release tablet:- In 15 minutes.

8. 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±0.5ºC. The tablets are kept in the cylindrical basket or directly placed in medium with paddle then rotated at 50 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 10ml. These samples were analyzed by uv spectrophotometry 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.

9. Stability study

Drug decomposition or degradation occurs during storage, because of chemical alteration of the active ingredients or due to product instability, lower the concentration of the drug in the dosage form. Stability study of the dosage form must include a section for product characterization and another section to study the product stability during storage. Formulations are evaluated for their appearance, possible weight gain in drug content thickness, flatness, folding endurance, tensile strength, moisture content and moisture uptake, and in-vitro release study by keeping dosage form in different temperature and humidity condition after a specified time. The stability study indicates that the formulation is quite stable at different conditions of storage. Recommended long-term and accelerated storage conditions Study Storage condition Minimum time period covered by data at submission. Long term-25°C ± 2°C/60% RH ± 5% RH or 30°C ± 2°C/65% RH ± 5% RH 12 months Intermediate-30°C ± 2°C/65% RH ± 5% RH 6 months Accelerated-40°C ± 2°C/75% RH ± 5% RH 6 month.

CONCLUSION

Immediate release is new enhanced oral product arising within this market segment and applicable to a wide range of therapeutic agents. 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. Some time immediate onset of action is desirable, to fulfill these medical needs, formulators have devote considerable effort to develop a novel type of tablet dosage form for oral administration, one that disintegrates and dissolves rapidly with enhanced dissolution. 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. An extension of marketexclusivity, which can be provide by immediate release dosage form, leads to increased revenue, while also targeting underserve and undertreated patient populations.

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