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IMMEDIATE RELEASE ORAL SOLID DOSAGE FORMS: A REVIEW

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Abstract:
Recently, Immediate release dosage form have taken over an important position in the market by overcoming previously administration problems and contributing to extension of patient life, which have difficulty in swallowing tablets and capsules. Many drugs belongs to BCS class2 having poor solubility in water need to be improvement in solubility and dissolution rate for enhancing its oral bioavailability, Although in many cases immediate onset of action is required than conventional therapy. Immediate release dosage form includes tablets, capsule, pellets, microsphere, granules, etc, among all these dosage from Tablet is more widespread dosage form.
The basic approached of development of tablet use of superdisintegrants like cross linked carboxymelhyl cellulose (Croscarmeliose), Sodium starch glycolate (Primogel, Explotab), Polyvinylpyrrolidone (Polyplasdone) etc. which provide instantaneous disintegration of tablet after administration. Various techniques are implemented to developed immediate release dosage form. The present review highlights on the prospective advantages, design and development of robust, stable, and orally immediate release as a pharmaceutical dosage form.
Key words: *Immediate release dosage form, tablet, polymer, superdisintegrants, etc.*

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INTRODUCTION:

Oral route is general route of drug administration because of its ease of ingestion, high-precision dosing, systemic effect, patient compliance, less expensive to manufacture. In most of conditions, immediate on set of action is essential comprise with to conventional treatment. To accomplish the quick onset of action and reduce the problems with conventional treatment immediate release dosage form is now a days popular oral dosage form. Immediate release dosage form is required for drugs having extensive biological half - life, high bioavailability, lower clearance and lower elimination half -life. But main condition for immediate release dosage form is poor solubility of the drug and need the immediate action of drug [1]. Pharmaceutical products intended for oral delivery and presently accessible on the prescription and over-the-counter markets are generally the immediate release type, which are intended for immediate release of drug for quick absorption. Disintegrating agents are materials regularly involved in tablet preparations and in some hard shell capsule formulations to help moisture permeation and diffusion of the medium of the dosage form in dissolution fluids. Super-disintegrant develops disintegrant efficiency resulting in decreased use levels when compared to traditional disintegrants [2]. An immediate release drug delivery permits a producer to prolong market exclusivity, though offering patients a suitable dosage form or dosage regimen. Recently immediate release tablets have started achieving popularity and acceptance as a drug delivery system. They are also a tool for growing markets, prolonging product life cycles and generating opportunities [3]. An Immediate release tablet are those, which disintegrate fast in saliva even absence of water. This might improve drug clinical effect through pre-gastric absorption from mouth, pharynx and esophagus by escaping first pass metabolism[4]. Whenever a solid dosage form is orally administered, the drug substance has to be dissolved first so that it can be absorbed[5]. For years, the most widespread dosage forms have been the solid, immediate release oral tablets and capsules. Normally, they comprise of a granular physical structure compounded by blending and compressing drug and excipient particles. The microstructure and solid-state properties are critical, for they identifying the rate of drug release in the gastrointestinal tract, showing the concentration profile of drug at the biological object. After incorporation, the granular, immediate-release dosage form is permeated by gastric fluid and the bonds among the particles are split resulting in fast disintegration of the dosage form into its particulate elements. The small drug particles with large surface area-to-volume ratio then discharge drug molecules and are dissolved almost immediately [6]. Many drugs belongs to BCS class2 having poor solubility in water need to boost the solubility and dissolution rate for increasing its oral bioavailability, on the other hand in various conditions, immediate onset of action is required than conventional treatment. 'Immediate release dosage' form 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. The word immediate release pharmaceutical preparation contains any formulation in which the frequency of release of drug from the product and/or the absorption of drug, is neither significant, nor intentionally, delayed by galenic operations. In the present case, immediate release may be delivered for by way of a suitable pharmaceutically satisfactory diluent or carrier, which diluent or carrier does not delay, to an appreciable extent, the rate of drug release and/or absorption [7]. Pellets are small, free flowing, spherical or semi-spherical solid particulate, generally in range 0.5 mm to 1.5 mm, and introduced commonly for oral administration, prepared by the agglomerates of fine powders or granules of bulk drugs and excipients using applicable processing equipment. Pellets can be prepared by more technique, the compaction and drug layering being the most widely used today [8]. The interest in pellet as drug delivery like (filled into capsule or compressed into disintegrating tablets) has been growing constantly, as their multiparticulate environment gives many important pharmacological as well as technological applications over conventional single unit formulations [9]. Pelletization or granulation process is process of forming spherical macro-particles by reducing moist particulate fine with help of adding of binder and other additives, in different pelletization method. Various pelletizing techniques are as follow: Extrusion spheronization, Layering Technique, Cryopelletization, Hot Melt Extrusion, Freeze Pelletization [10].

Microspheres are normally free flowing powders containing of spherical particles of size less than 200 µm. can be inserts by 18 or 20 digit needle. They involves proteins or synthetic polymers which are biodegradable in environment. A well designed controlled drug delivery system can overcome some of the problems of conventional treatment and improve the therapeutic efficacy of a given drug [11].

Microspheres can be prepared by Emulsion solvent evaporation technique, Emulsion cross linking method, Coacervation method, Spray drying technique, Emulsion-solvent diffusion technique, Multiple emulsion method, Ionic gelation, Hydroxyl appetite (HAP) microspheres in sphere morphology [12].

Immediate release drug-delivery systems were first established in the late 1970s as an alternative to tablets, capsules, and syrups for pediatric and geriatric patients who experience problems in swallowing traditional oral solid-dosage forms. Oral films, also known as oral wafers, Dissolvable oral thin films (OTFs) or oral strip (OS) developed over the past few years from the confection and oral care markets in the form of breath strips and became a novel and widely accepted form by consumers for delivering vitamins and personal care products[13]. Whenever it interact with saliva, within a few sec it dissolved, water is not required for that, making them predominantly appropriate for pediatric and geriatric patients. As most of the polymers used in mouth dissolving films (MDFs) are amorphous, dispersion of drug in polymer matrix aids rapid dissolution. These advantages enhance the patient compliance and make pharmaceutical manufacturer invest money in change of the existing products in the market to MDFs[14]. Oral dissolving films are immediate disintegrating thin films having an area ranging from 5 to 20 cm2 in which drug is combined in the form of matrix with hydrophilic polymer. Active pharmaceutical ingredient can be integrated up to 15 mg along with other additives i.e., plasticizers, colorants, sweeteners, taste masking agents etc. Plasticizer enhances workability, spreadability and flexibility of films thus decreasing the glass transition temperature of polymers. Conventional approach of preparing oral dispersible film is solvent casting method, semisolid casting method, hot melt extrusion method, solid dispersion extrusion, rolling method, spray technique, etc.[15].

BIOPHARMACEUTICAL CONSIDERATION:

Pharmacokinetics:

In this aspect, study has done on absorption, distribution, metabolism and excretion. After absorption, drug attains therapeutic level and therefore produces pharmacological response, hence both rate and extend of absorption is important. In conventional drug therapy there is delay in disintegration and hence dissolution. While immediate dosage form is rapidly disintegrating in oral cavity and dissolution is fast. Due to disintegration of RDT in mouth absorption in started from mouth, pharynx and esophagus. Some factors like age, GI pH, and blood flow by GI are taken into consideration, because elders may be denoted as distinct unique Medicare population. Drug distribution carried out by tissue permeability, perfusion rate, binding of drug to tissue, disease state, drug interaction etc. In geriatric patients, decrease in body mass and total body water result in decreased volume of distribution of water-soluble drugs and increased volume of distribution (Vd) of lipid soluble drugs. Excretion by renal clearance is slowed, thus half-life of renal excreted drugs increase [16].

Pharmacodynamics:

Decreased capacity of the body to react baro reflexive stimuli, cardiac output, and orthostatic hypotension may see in taking antihypertensive like prazosin.

Decreased sensitivity of the CVS to b-adrenergic agonist and antagonist. Immunity is less and taken into consideration while administered antibiotics.

Different reaction to drug treatment-elderly indicate reduced bronchodilator effect of theophylline shows increased sensitivity to barbiturates [17].

Advantages of immediate release oral solid dosage form:

Improved patient compliance due to ease of administration in case of dysphagic patient.
Stability, bioavailability increase with the immediate release dosage form through transmucosal delivery and pregastric absorption.

Unit dose system and have a long shelf life.
It should be appropriate for controlled or sustained release targets.
Maximum drug loading is possible with immediate release.
Ability to provide advantages of liquid medication in the form of solid preparation.
Cost effective because manufacturing process is easy therefore less expensive.
Increased in solubility of pharmaceutical composition.
Due immediate release of drug delivery that decreases the drug disintegration and dissolution time.
Immediate dosage form are much effective in lower concentration.
Immediate release dosage forms are those for which ≥85% of labelled amount dissolves within 30 min [18, 19].

Disadvantages of immediate release oral solid dosage form:

Swallowing of solid dosage form such as tablet and capsule produce difficulties with pediatric and geriatric patients due to incomplete development of

muscular and nervous system or suffer from dysphagia.
Chance of gastro-intestinal irritation for high concentration medicaments, because of physical obstacles and adherence to an esophagus may cause gastrointestinal ulceration.
Drug release at a time can make high plasma concentration which leads to toxicity.
The drug having short half-life that create problem such as frequent dosing [20].

Ideal characteristic for immediate release drug delivery system:
Ease of administration to patients who refuse to swallow a tablet, such as pediatric and geriatric patients and, psychiatric patients
It should dissolve or disintegrate in the stomach within a short period in the case of solid dosage.
It should not leave minimal or no residue in the mouth after oral administration.
Immediate release dosage form of drug should show first absorption and then dissolution of drug.
Exhibit low sensitivity to environmental condition as humidity and temperature.
Faster dissolution and absorption of drug that produces the rapid onset of action.
It should have ability to have properties like taste masking.
Immediate solid dosage form should provide pleasant mouth feel.
It should be manufactured using conventional processing and packaging equipment at low cost.
Allow the making of tablet using conventional method and packaging equipment's .
Immediate dosage form should have ability to deliver advantages of liquid medication in the form of solid preparation.
[21, 22, 23].

Tablets:
Tablets are the pharmaceutical solid dosage forms consisting of drug constituents with or without appropriate diluents and prepared by compression as well as molding techniques. They are a unit dose form, and they shows the highest capabilities of all oral dosage forms for the maximum dose precision and the smallest content variability and are lightest and most dense of all oral dosage forms. Tablet may be uncoated or coated. Uncoated tablets are effervescent tablet, chewable tablet, soluble tablet, lozenge tablet, and sublingual tablet. Coated tablets are film coated tablet, enteric coated tablet, implant, modified-release tablet and sugar coated tablet [24].

Types of Immediate release tablets:
Orally ingested tablets:
Compressed tablets
Multiple compressed tablets
Layered tablets
Compression-coated tablets
Repeat-action tablets
Delayed-action and enteric-coated tablets
Sugar and chocolate-coated tablets
Film coated tablets
Chewable tablets

Tablets Used in the Oral Cavity
Buccal tablets
Sublingual tablets
Troches and lozenges
Dental cones

Tablets Administered by Other Routes
Implantation tablets
Vaginal tablets

D. Tablets Used to Prepare Solutions
Effervescent tablets
Dispensing tablets
Hypodermic tablets
Tablet triturates [25, 26].

Excipients used in immediate release dosage form:
In Immediate release dosage form excipients balance characteristics of active ingredients. This demands a detailed understanding of the interaction of these excipients to avoid contact with the actives. The role of additives is significant in the formulation of quick-dissolving tablets. When inactive food grade ingredients is incorporated in the formulation that gives the desired organoleptic characteristics and efficacy of product [27]. Mainly excipients used in immediate release drug delivery are as follow at least on disintegrant, a diluents, a lubricants, and optionally sweeteners, swelling agents and flavoring agents etc. The temperature of the excipients should be preferably around 30–350C for fast dissolving properties [28].

Bulking agents:
Bulking agents are significant used in the formulation of rapid dissolving tablets. The material contributes elements of a diluents, filler and cost reducer. Bulking agents increases the textural properties that in turn developed the disintegration in the mouth, other than; adding bulk also lessen the concentration of the active in the composition. The recommended bulking material for this delivery system should be more sugar-based. Ex. Mannitol, polydextrose, lacitol etc. [29].

Lubricants:
Lubricants, although it is not crucial excipients, can further help in building these tablets more edible after they disintegrate in the mouth. Lubricants eliminate grittiness and help in the drug transport mechanism from the mouth down into the stomach [30].

Emulsifying agents:
Emulsifying material are important excipients for making immediate release dosage form they help in rapid disintegration and drug release without chewing, swallowing or drinking water. In addition, incorporating emulsifiers is useful in stabilizing the immiscible blends and improving bioavailability. A wide range of emulsifiers is recommended for fast-tablet formulation, including alkyl sulfates, propylene glycol esters, lecithin, sucrose esters and others. These materials can be added in the range of 0.05 % to about 15 % by weight of the final composition [31].

Flavors and Sweeteners:
The product with flavors and taste masking agents should prepare product most palatable and pleasing for patients. The incorporation of these agents supports in overcoming bitterness and undesirable tastes of some active ingredients. For immediate release tablet to enhance the organoleptic characteristic, both synthetic and natural flavors can be used. Ex. Sugar, dextrose, mannitol. Incorporation of sweeteners contribute to pleasant taste as well as bulk to the composition [32].

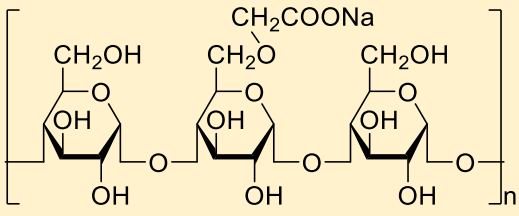
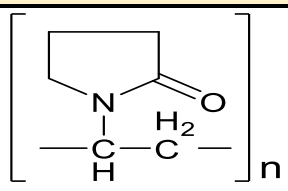
Superdisintegrants:
Disintegrants are agents regularly incorporated in tablet formulations and in certain hard shell capsule preparations to stimulate moisture diffusion and dispersion of the matrix of dosage form in dissolution fluids. At low concentration, superdisintegrants usually used, typically 1-10percent by weight relative to total weight of dosage unit. Commonly used superdisintegrants are croscarmellose sodium (Aci-di-Sol), crospovidone (CP), etc. Primarily, superdisintegrants can cause tablet to burst into granules from which it was been compressed as well as fine powder from which granules were prepared [33].

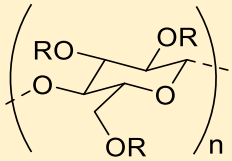
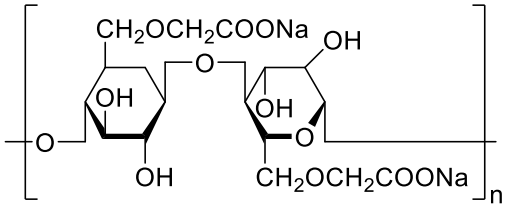
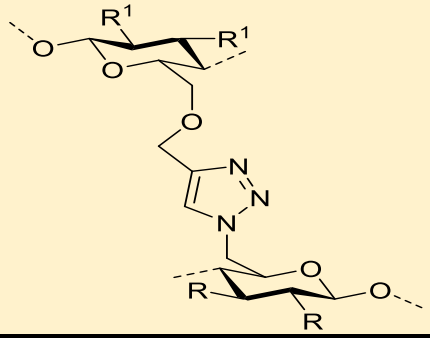
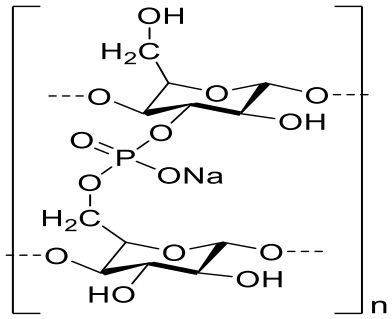
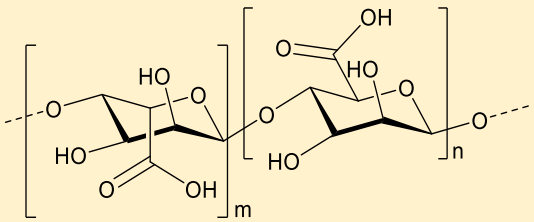
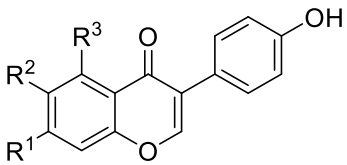
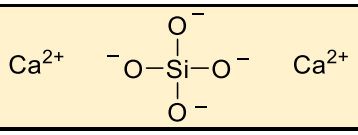
Selection of superdisintegrant:
Even though superdisintegrants principally affect the rate of disintegration, numerous ideal elements to be considered during selection of an applicable superdisintegrants for a specific formulation should:
When tablet moves towards saliva in the mouth/oral cavity, that produces prompt disintegration.

It should be compactable enough to make less friable tablets.

Due to fine particle size is ideal to attained patient compliance, and thus that gives the good mouth feel to patients [34].

Table no. 1 list of Super disintegrants

Super disintegrants	Mechanism of action	Chemical structure
Sodium Starch Glycolate	Rapid and extensive swelling with minimal gelling. Microcrystalline cellulose (Synonym: Avicel, celex) used in concentration of 2-15% of tablet weight. And Water wicking	
Cross-linked Povidone or crospovidone	Swells very little and returns to original size after compression but act by capillary action.	

Hydroxyl propyl cellulose	Certain grades can also provide some binding properties while retaining disintegration capacity. Recommended concentration 1-5%	 R=H or $CH_2CH(OH)CH_3$
Croscarmellose sodium	Wicking due to fibrous structure, swelling with minimal gelling. Effective Concentrations: 1-3% Direct Compression, 2-4% Wet Granulation	
Crosslinked cellulose	Swells 4-8 folds in < 10 seconds. Swelling and wicking both.	
Crosslinked starch	Swells 7-12 folds in < 30 seconds.	
Crosslinked alginic acid	Rapid swelling in aqueous medium or wicking action.	
Soy polysaccharides	It is a natural super disintegrant that does not contain any starch or sugar so can be used in nutritional products.	
Calcium silicate	Wicking action.	

Mechanism of superdisintegrants:

For tablet disintegration there are four major mechanism are as follow:

Swelling

Porosity and capillary action

Due to disintegrating particles or repulsive forces

Due to deformation

Swelling: The most extensively accepted broad-spectrum mechanism of action for disintegration of tablet is swelling. Tablets displays poor disintegration with high porosity due to absence of sufficient swelling force. As well as, adequate swelling force is employed in the tablet with low porosity. It is valuable to note that if the packing fraction is very high, fluid is incapable to enter into the tablet and disintegration is again slows down [35].

Porosity and capillary action/ wicking action:

First step in the capillary action is always the disintegration. Active disintegrants that cannot swell are supposed to apply their disintegrating action with the help of porosity and capillary action.

When we place the tablet into appropriate aqueous medium, the medium enters into the tablet and exchanges the air adsorbed on the elements, which weakens the intermolecular bond and breaks the tablet into fine particles. Water uptake by tablet is determined by hydrophilicity of the drug or excipient and on tableting situations. For these types of disintegrants maintenance of porous structure and low interfacial tension towards aqueous fluid is essential which supports in disintegration by generating a hydrophilic network around the drug particles [36].

Due to disintegrating particle or repulsive forces:

Alternative mechanism of disintegration tries to describe the tablet swelling prepared with 'nonswellable' disintegrants. Guyot-Hermann has discovered a particle repulsion theory based on the observation that nonswelling particle also cause disintegration of tablets. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it. Researchers found that repulsion is secondary to wicking [37].

Due to deformation:

Starch grains are generally thought to be "elastic" in nature meaning that grains that are deformed under pressure will return to their original shape when that pressure is removed. But, with the compression forces involved in tableting, these grains are believed to be deformed more permanently and are said to be "energy rich" with this energy being released upon exposure to water. In other words, during compression of tablet, disintegrated particles become deformed and these deformed particles get into their regular structure when they come in contact with aqueous media or water. Sometimes, the swelling ability of starch was enhanced when granules were broadly distorted while compression. This increase in size of the deformed particles produces a breakup of the tablet [38, 39].

Role of superdisintegrants:

Superdisintegrants allows rapid disintegration owing to combine outcome of swelling and absorption of water by the formulations.

The wetted surface of carriers increases due to swelling of superdisintegrants; this enhances the wettability and dispersibility of system hence promoting the dissolution and disintegration.

Superdisintegrante"s are selected according to critical concentration of disintegrant. Below this concentration, the tablet disintegration time is inversely proportional to the concentration of the superdisintegrant, whereas if concentration of super disintegrant is above critical concentration, the disintegration time remains almost constant or even increases [40].

Method of preparing immediate release dosage form:

Immediate release tablet can be prepared by following technique:

Tablet molding technique

Wet granulation technique

Direct compression technique

By solid dispersions

Mass extrusion technique

Tablet molding technique:

In this technique, molded tablets are manufactured by using water-soluble ingredients so that the tablets dissolve entirely and quickly [41]. Tablet molding process is of two types i.e. solvent method and heat method. Solvent method includes moistening the powder blend with a hydro alcoholic solvent followed by compression at low pressures in molded plates to form a wetted mass (compression molding). The solvent is then removed by air-drying. The heat molding process involves preparation of a suspension that contains a drug, agar and sugar (e.g. mannitol` or lactose) and pouring the suspension in the blister packaging wells, solidifying the agar at the room temperature to form a jelly and drying at 30˚c under vacuum [42]. Molded tablets disintegrate more rapidly and offer improved taste because the dispersion matrix

is in general made from water soluble sugars. The active ingredients in most cases are absorbed through the mucosal lining of the mouth. Unluckily, moulded tablets typically do not possess great mechanical strength. Erosion and breakage of the moulded tablets often occurs during tablet handling and when blister pockets are opened. Hardness agents can be added to the formulation, but then the rate of tablet solubility usually decreases [43].

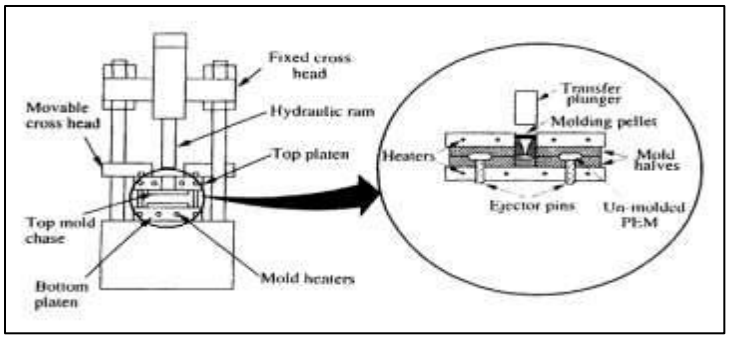


Figure 1. Tablet Molding Technique

Wet granulation technique:

Wet granulation is a usually used unit operation in the pharmaceutical industry. Wet granulation is frequently carried out utilizing a high-shear mixer. The high-shear granulation method is a rapid process which is prone for over wetting. Hence, the liquid volume added is critical and the optimum amount is affected by the characteristics of the raw materials. Power intake of the impeller motor and the impeller torque have been applied to monitor the rheological characteristics of the wet mass while agglomeration and thus, have been used to determine the end-point of water addition. Although, these techniques are affected by the equipment variables. Therefore, other procedure monitoring method should be appreciated. Significant steps included in wet granulation are as follow:

Mixture of drug and excipients. Preparing the solution of binder then mix the powder with binder solution to form a wet mass. Coarse screening of wet mass with help of appropriate sieve (6 to 12) screen. After that dry the moist granules, by using proper sieve (14 to 20) screening of dry granules is done. Mixing of screened granules with glidant, disintegrant, and lubricant.

Advantages:
Wet granulation is rapid process.
These technique have ability operated continuously.
Appropriate for heat sensitive preparation.
Disadvantages:
Wet granulation is process which required high cost, it is very expensive because of time, labor, energy, equipment, and space requirement [44].

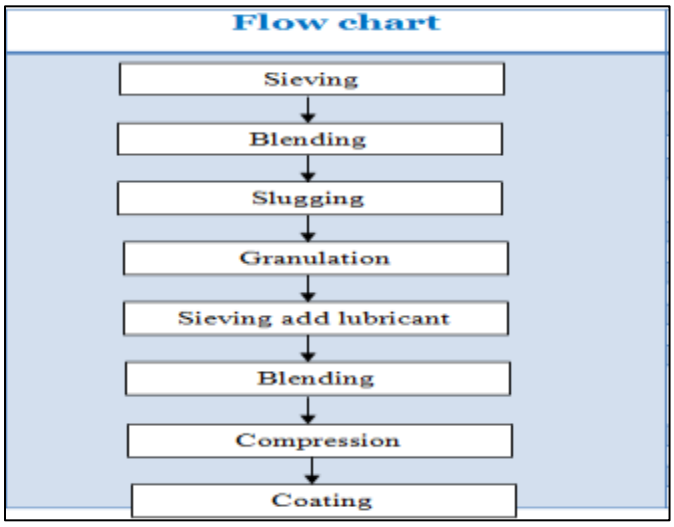


Figure 2. Wet granulation technique

Direct compression technique:

Direct compression is the easiest way to manufacturing of tablet. In this techniques, without any primary treatment, tablets are compressed directly from the mixture of drug and excipients. No pre-treatment of the powder mixture by wet or dry granulation procedure is necessary. Between the methods used to prepare tablets, direct compression is the most progressive technology. It includes only blending and compression, hence presenting advantage mainly in terms of immediate production, as it needs less unit operations, fewer machinery, and cheap number of personnel and significantly less processing time along with increased product stability.

Advantages:

Direct compression is much more effective and economical method as compared to other procedures, because it includes only dry blending and compaction of API and essential
excipients.

The significant benefit of direct compression is that it is an inexpensive process.

less processing time, reduced labour costs, limited manufacturing steps, low manufacturing cost and less number of equipments is essential, less process validation, reduced consumption of power.

It is vital to select a appropriate and an ideal concentration of disintegrant to confirm rapid disintegration and dissolution.

In case of directly compressed tablets after disintegration each primary drug particle is
liberated. Whereas in the case of tablets formulated by compression of granules small drug
particles with a larger surface area adhere together into larger agglomerates, thus decreasing
the surface area available for dissolution [45, 46].

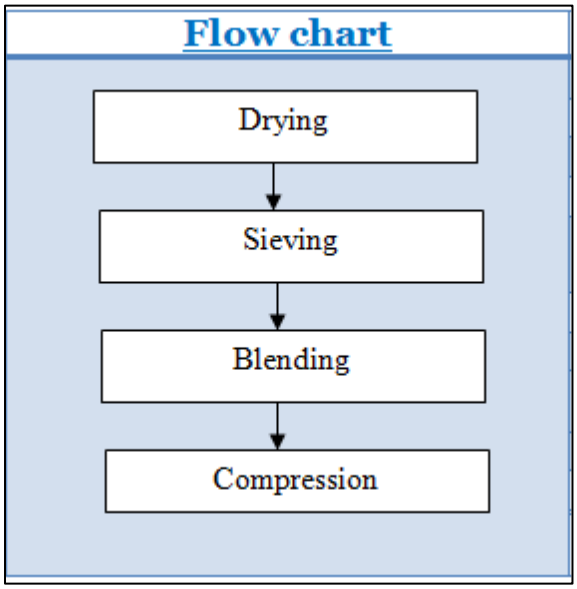


Figure 3. Direct compression technique

By solid dispersion:

When preparing immediate release solid dosage forms from solid amorphous dispersion for oral drug delivery to a utilize nature like the GI tract of an animal such as a human, it is frequently required to maximize the extent of dispersion present in the dosage form. This reduces the size of the solid dosage form necessary to accomplish the desired dose. The immediate release dosage forms containing a solid dispersion that improves the solubility of a "low-solubility drug," that means 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," means, it has an aqueous solubility about 1 to 2 mg/mL, or low to moderate aqueous-solubility, having an aqueous-solubility from about 1 mg/mL to as high as about 20 to 40 mg/mL. At least one concentration enhancing polymer and drug dispersion can be used in producing high loading immediate release dosage form of current discovery comprises solid dispersion of drug. At a minimum, the dispersions utilized in the current discovery offer concentration enrichment relative to a control containing of crystalline drug alone. Hence, the concentration-enhancing polymer is present in a adequate amount so that when the dispersion is delivered to a use environment, the dispersion offers improved drug concentration relative to a control consisting of an equivalent amount of crystalline drug, but with no concentration-enhancing polymer present [47].

Mass extrusion:
In this technique active mixture is softened by the solvent mixture of water-soluble polyethylene glycol and methanol and then subsequent expulsion of softened mass through the extruder or syringe is made to get a cylinder of the product into even segments using heated blade to form tablet. The dried cylinder can also be used to coat granules for bitter drugs and thereby achieve taste masking [48, 49].

Evaluations of powder blend:
Angle of repose:
It is defined as the maximum angle possible among the surface of the pile of the powder and the horizontal plane. It is determined by

$$(\theta) = tan^{-1}\frac{h}{r} \qquad (1)$$

h = Height of cone
r = Radius of the cone base
θ = Angle of repose
Angle of repose is less than 30, indicates the free flowing properties of the material.
Flow properties are measured by angle of repose [50].

Bulk density:
Weight per unit volume is known as density. Bulk density (P_b) is the mass of powder divided by bulk volume and is expressed as gm/cm$^{3.}$ The bulk density of a powder principally depends on particle size distribution, 'particle shape and the affinity of particles to adhere together. There are two kinds of bulk density. Weighed quantity of sample was poured into measuring cylinder and Volume (Vo) was noted [51].

$$Bulk\ density\ = \frac{W}{Vo} \qquad (2)$$

Where,
W= weight of powder
Vf = Initial volume of powder

Tapped density:
Weighed amount of sample were poured in measuring cylinder then cylinder was fixed into density apparatus and for 100 tapping the timer knob is set. After that measuring of volume (Vf). And the procedure will be continued until 2 consecutive reading were same.

The tapped density were calculated as follow:

$$Tapped\ density\ = \frac{W}{Vf} \qquad (3)$$

Where,
W= weight of powder
Vf = final volume of powder.

Carr's Compressibility Index:
Flow ability of powder or compressibility index can be determine by using Carr's index. This can be calculated with the help of bulk density and tapped density, it can be denoted as percentage. The theory explain, the less compressible a material the more flow able it is.

Carr's index can be calculated as follow:

$$Carr's\ Index\ =\ Tapped\ density - bulk\frac{density}{Tapped\ density} * 100 \qquad (4)$$

Hausner's ratio:
Hausner's ratio determined the flow characteristics of powder blend and it is calculated by taking ratio of tapped density to bulk density [52].

$$Hausner's\ ratio\ =\ Tapped\frac{density}{Bulk\ density} \qquad (5)$$

Evaluations of Immediate release Tablets:
Immediate release tablet can be evaluated by using parameter such as thickness, hardness, friability, weight variations, drug content, disintegration time, In vitro Drug release study, and stability.

Thickness:
Tablet thickness can be measured with the help of vernier calipers. Thickness can be measured in mm. select 10 tablets randomly and measured for thickness that shown as$Mean\ \pm\ SD$.

Hardness:
By using suitable apparatus hardness is measuring the force required to break the tablet. Randomly choose the 10 tablets from whole batch for hardness testing with help of various hardness tester like Monsanto hardness tester, Pfizer hardness tester. Hardness measured in kg/cm$^{2.}$

Friability:
Measurement of tablets friability enhancements other physical strength dimension, such as tablet crushing strength. Friability of tablet is determined for to ensure that tablets are stable to abrasion or not. Friability test can be done by using apparatus known as Roche friabilator. Randomly weighed 20 tablets and are kept in plastic rotating drum attached to the device rotated for 100 revolution at 25 rpm. After that tablets are weighed again, % Friability is calculated as follow:

$$\%\ Friability\ =\ (Wo\ -\ W)/\ Wo * 100$$

Where,
Wo = Initial weight of 20 tablets.
W = Weight after 100 revolution.
The weight loss would not be more than 1 percentage w/w.

Weight variation:
Weight variation can be done in order to demonstrate uniformity in tablets weight in a batch.
Randomly weight 20 tablets individually from complete batch and average weight should be calculated. Then comparison is done between Individual tablets weight and average tablet weight. According to USP, more than two tablets would not drop outside percentage limit and no tablet must not varies by more than two times the %limit [53].
$PD\ =\ [(Wavg\ -\ Winitial)/\ (Wavg)] * 100]$

Drug Content:
Powdered 10 tablets and 100mg drug equivalent powder dissolved in appropriate media (buffer and 0.1N HCL). Volume make up to 100ml by this media, solution was filtered and diluted 100times and examined spectrophotometrically and further calculation carried out to detected drug content in 1 tablet.

Disintegration test:
Disintegration apparatus is required to carried out disintegration test. Placed 6 tablets in 6 tube of apparatus 1 tablet in each tube, use disk if prescribed. Distilled water is used as disintegration media, maintained at 37˚C ± 2˚ in immersion fluid. Proceed the device until each of the unit dosage form come out of the basket, 15mins for uncoated tablets, plain tablets required 30mins, 60mins for coated tablets and pills.

***In vitro* drug release study:**
In vitro drug release can be determine with the help of apparatus known as Dissolution apparatus. Contain dissolution media of volume 900ml and maintained at 37˚ ± 0.5˚C. Tablets are placed in cylindrical basket or directly kept in media and instantly run the device at appropriate rate. Within the time intermission specified (5, 10, 15 and 30min) or at each time interval withdraw the sample from midway of dissolution medium and top of the rotating basket, not less than 10mm from vessel wall and replace the same volume of fresh media. The samples are filter and from the filtrate 1ml is taken and dilute to 10ml. The sample was examined and then calculated to get a 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.

Stability study:
The ICH Q1A, Q1B, Q1C, and Q5C are publications on stability. Purity, potency, and safety of drug product is depends on stability of dosage form.

Stability can be done on formulation, drug product and packaged product. Stability testing thus permits to the creating of mentioned storage conditions, retest periods, and eventually product shelf life and expiry dating. To evaluating the stability of drug product blend of temperature and humidity is required. In storage chamber temperature must be controlled within ±2°C, and the humidity controlled within ±5% relative humidity. There are 3 storage condition of stability are Intermediate condition (30°C ± 2 °C / 65% RH ±5% RH), accelerated condition (40°C ± 2°C / 75% RH ±5% RH), Long term stability study(25 °C ±2 °C / 60% RH ±5% RH or 30 °C ±2 °C / 65% RH ±5% RH or 30 °C ±2°C / 75% RH ±5% RH) [54].

Table no. 2 various immediate release dosage form with their therapeutic areas.

Therapeutics area	Immediate release dosage forms
Analgesics and Anti-inflammatory Agents	Ibuprofen, Indomethacin, Ketoprofen, Meclofenamic Acid,
Anthelmintics	Albendazole, Mebendazole, Oxantel,Embonate,Thiabendazole.
Anti-Arrhythmic Agents	Amiodarone Hcl, Disopyramide
Anti-bacterial Agents	Penicillin, Ciprofloxacin HCl, Clarithromycin, Doxycycline, Erythromycin, Nalidixic Acid, , Rifampicin,
Anti-coagulants	Dicoumarol, Dipyridamole
Anti-depressants	Amoxapine, Ciclazindol, Maprotiline HCl, Mianserin HCl,Trazodone HCl.
Histamine H,-Receptor Antagonists	Cyclizine, cyproheptadine HCl, dimenhydrinate, flunarizine HCl
Anti-diabetics	Acetohexamide, Chlorpropamide, Glibenclamide,Gliclazide
Gastro-intestinal Agents	Cimetidine, cisapride, diphenoxylate HCl,famotidine
Diuretics	Acetazolamideamiloride, bendrofluazide, bumetanide, chlorothiazide
Cardiac InotropicAgents	Amrinone, Digitoxin, Digoxin, Enoximone

Table no. 3 various immediate release dosage form with marketed preparation

Brand name	Generic name	Disease / indication	Dose	Dosage form
PROVACHOL®	*Pravastatin*	Cholesterol & Fast	20mg/80mg	Tablet
DIAVON®	Valsartan	Anti-hypertensive	40mg/320mg	Tablet
Advil®	Ibuprofen	NSAID	800mg/300mg	Tablet

Abilify Among®	Aripiprazole	antipsychotic	30mg/2mg	Tablet
Albenza®	Albendazole	Anthelmintics	800mg/ 400mg	Tablet
Cipro XR®	Ciprofloxacin HCl	Anti-bacterial Agents	500mg/250mg	Tablet
COUMADIN®	Warfarin	Anti-coagulants	10mg/2mg	Tablet
Asendin	Amoxapine	Anti-depressants	1to 3 tab./day	Tablet/ Capsules
Valoid®	Cyclizine	Histamine H, Receptor Antagonists	50mg	Tablet
Daonil	Glibenclamide	Anti-diabetics	1.25mg/5mg	Tablet
Tagamet	Cimetidine	Gastro-intestinal Agents	400mg/200mg	Tablet
Procardia, Procardia LX	Nifedipine	Anti-hypertensive	60mg/30mg	Tablet
Trexall	Methotrexate	Antineoplastic agent	10mg/30mg	Tablet

DISCUSSION:

Based on literature survey it is reported that, Immediate release dosage form is, 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. Immediate release may be provided 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 dosage form includes, Tablets, capsules, pellets, granules, microspheres, etc. Among all these dosage form tablet is most popular dosage form existing today because of its convenience of self administration, compactness and easy manufacturing; sometimes immediate onset of action is required than conventional therapy in many cases. Immediate drug release dosage forms disintegrate rapidly after administration with enhanced rate of dissolution. The development 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.

Excipients balance the properties of the actives in immediate release dosage forms. Superdisinegrants play a major role in the development of immediate release tablets, ex; Cross linked Polyvinylpyrrolidone or crospovidone (Polyplasdone), Sodium starch glycolate (Primogel, Explotab), carboxymethylcellulose (Croscarmellose) etc. There are different techniques which are utilized for manufacturing of immediate release tablets are Tablet molding technique, Wet granulation technique, Direct compression technique, By solid dispersions, Mass extrusion technique. This article also discusses the evaluation methodologies for these orally disintegrating tablets. Various modifications in the conventional evaluation and use of specialized instruments are found to be essential in the testing of these dosage forms. In the present review the formulation techniques and different technologies are discussed. The development of immediate release therapy also provides an opportunity for a line extension in the marketplace, a wide range of drugs e.g., neuroleptics, cardiovascular drugs, analgesics, antihistamines and other drugs can be considered candidates for this dosage form.

CONCLUSION:

Immediate release of dosage form is applicable to a wide range of therapeutic agents involving generics, therefore adding value, i.e. ‘supergenerics’ for veterinary or human application. Almost one-third of the patients required rapid therapeutic action of drug,

resulting in poor compliance with conventional drug treatment which leads to reduced overall treatment effectiveness. Sometime immediate onset of action is necessary, to accomplish these medical requirements, formulators have dedicate significant determination to improve a novel type of tablet dosage form for oral drug delivery, one that disintegrates and dissolves quickly with higher dissolution. The immediate release dosage form have combine benefits of easy administration of dosage form and compliance or convenience of dosing. These tablets are designed to release the medicaments with an enhanced rate. There are various techniques are developed above to improved manufacturing process for immediate release pharmaceutical product which are mechanically strong. An extension of market exclusivity, which can be provided by immediate release dosage form, leads to increased revenue, while also targeting underserved and under-treated patient populations.

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