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A Review on Immediate Release Drug Delivery System

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ABSTRACT

Most common and popular route of administration of drug is oral route. Tablet form is the most widely used dosage form because of self-administration and ease in manufacturing. 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 now a days popular and used as a alternative oral dosage form. Immediate release tablet are very quickly after administration. Basic approach used in development is the use of superdisintegrants which provide rapid disintegration of tablet after administration.

Keywords: immediate release, superdisintegrants,

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INTRODUCTION [1]

Oral route is most common and popular route of administration of drug is oral route because of its systemic effect, patient compliance, less expensive to manufacture. Tablet provides high precision dosing. Tablet form is the most widely used dosage form because of self-administration and ease in manufacturing. 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 now a days popular and used as a alternative oral dosage form. Immediate release tablet are very quickly after administration. Basic approach used in development is the use of superdisintegrants which provide rapid disintegration of tablet after administration.

TYPES OF TABLET:[2,3,4]

1. **Tablets ingested orally**
   a. Standard Compressed tablet
   b. Multiple compressed tablet
      (1) Layered Tablet
      (2) Compression coated Tablet
   c. Repeat action Tablet
   d. Delayed action and enteric coated Tablet
   e. Sugar and chocolate coated tablet
   f. Film coated tablet
   g. Chewable Tablet
   h. Targeted tablet
      (1) Floating tablet
      (2) Colon targeted tablet

These tablets are meant to be swallowed intact along with a sufficient quantity of potable water. Exception is chewable tablet. Over 90% of the tablets manufactured today are ingested orally. This shows that this class of formulation is the most popular worldwide and the major attention of the researcher is towards this direction.

2. **Tablets used in the oral cavity:**
   a. Buckle Tablet
   b. Sublingual Tablet
   c. Troches and Lozenges
   d. Dental cones
   e. Mouth dissolved tablet

The tablets under this group are aimed release API in oral cavity or to provide local action in this region. The tablets under this category avoids first-pass metabolism, decomposition in gastric environment, nauseatic sensations and gives rapid onset of action. The tablets formulated for this region are designed to fit in proper region of oral cavity.

3. **Tablets administered by other routes:**

a. Implantation Tablet
b. Vaginal Tablets

These tablets are administered by other route except for the oral cavity and so the drugs are avoided from passing through gastro intestinal tract. These tablets may be inserted into other body cavities or directly placed below the skin to be absorbed into systemic circulation from the site of application.

4. **Tablets used to prepare solution:**
   a. Effervescent Tablet
   b. Dispensing Tablet
   c. Hypodermic Tablet
   d. Tablets Triturates

IMMEDIATE RELEASE:[5,6]

The tablets under this category are required to be dissolved first in water or other solvents before administration or application. This solution may be for ingestion or parenteral application or for topical use depending upon type of medicament used.Immediate release tablets are those which disintegrate rapidly and get dissolved to release the medicaments. Immediate release may be provided for by way of an appropriate pharmaceutically acceptable diluent or carrier, which diluent or carrier does not prolong, to an appreciable extent, the rate of drug release and/or absorption. This term excludes formulations which are adapted to provide for “modified”, “controlled”, “sustained”, “prolonged”, “extended” or “delayed” release of drug.Release term includes the provision (or presentation) of drug from the formulation to the gastrointestinal tract, to body tissues and/or into systemic circulation. For gastrointestinal tract release, the release is under pH conditions such as pH=1 to 3, especially at, or about, pH=1. In one aspect of the invention a formulation as described herein with a compound of formula (I), or an acid addition salt thereof, in crystalline form releases drug under a range of pH conditions. In another aspect of the invention a formulation as described herein with a compound of formula (I), or an acid addition salt thereof, releases drug under pH conditions such as pH=1 to 3, especially at, or about, pH=1. Thus, formulations of the invention may release at least 70% (preferably 80%) of active ingredient within 4 hours, such as within 3 hours, preferably 2 hours, more preferably within 1.5 hours, and especially within an hour (such as within 30 minutes), of administration, whether this be oral or parenteral.

IMMEDIATE RELEASE FILM COATED TABLETS:

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. 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.

PROBLEMS WITH EXISTING ORAL DOSAGE FORM:[7,8]

1. Patient may suffer from tremors therefore they have difficulty to take powder and liquids. In dysphasia physical obstacles and adherence to an esophagus may cause gastrointestinal ulceration.
2. Swallowing of solid dosage forms like tablet and capsules and produce difficulty for young adult of incomplete development of muscular and nervous system and elderly patients suffer from dysphasia.
3. Liquid medicaments (suspension and emulsion) are packed in multidose container; therefore achievement of uniformity in the content of each dose may be difficult.
4. Buccal and sublingual formation may cause irritation to oral mucosa, so patients refused to use such medications.
5. Cost of products is main factor as parenteral formulations are most costly and discomfort.

DESIRED CRITERIA FOR IMMEDIATE RELEASE DRUG DELIVERY SYSTEM:[9,10]

Immediate release dosage form should:

1. In the case of solid dosage it should dissolve or disintegrate in the stomach within a short period.
2. In the case of liquid dosage form it should be compatible with taste masking.
3. Be portable without fragility concern.
4. Have a pleasing mouth feel.
5. It should not leave minimal or no residue in the mouth after oral administration.
6. Exhibit low sensitivity to environmental condition as humidity and temperature.
7. Be manufactured using conventional processing and packaging equipment at low cost.
8. Rapid dissolution and absorption of drug, which may produce rapid onset of action.

MERITS OF IMMEDIATE RELEASE DRUG DELIVERY SYSTEM:[11]

1. Improved compliance/added convenience
2. Improved stability, bioavailability
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
8. Improved solubility of the pharmaceutical composition
9. Decreased disintegration and dissolution times for immediate release oral dosage forms

PHARMACOKINETICS:[7,8,9,10]

It is the study of absorption, distribution, metabolism and excretion. After absorption, drug attains therapeutic level and therefore elicits pharmacological effect, so both rate and extend of absorption is important. In conventional dosage form there is delay

in disintegration and therefore dissolution is fast. Drug distribution depends on many factors like tissue permeability, perfusion rate, binding of drug to tissue, disease state, drug interaction etc.

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

PHARMACODYNAMIC:

- Drug reception interaction impaired in elderly as well as in young adult due to undue development of organ.
- Decreased ability of the body to respond reflexive stimuli, cardiac output, and orthostatic hypotension may see in taking antihypertensive like prazosin.
- Decreased sensitivity of the CVS to 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 d*epends on disease state of the patient.

EXCEPIENTS:[12]

Bulking agent, emulsifying agent, lubricant, flavors and sweeteners and most important excipient in immediate release is super disintegration.

SUPER DISINTEGRATION:

A disintegrant is an excipient, which is added to a tablet or capsule blend to aid in the break up of the compacted mass when it is put into a fluid environment.

Advantages:

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

Some super disintegrants are:

- Sodium Starch Glycolate (Explotab, primogel) used in concentration of 2-8 % & optimum is 4%.

Mechanism of Action: Rapid and extensive swelling with minimal gelling. Microcrystalline cellulose (Synonym: Avicel, celex) used in concentration of 2-15% of tablet weight. And Water wicking

- Cross-linked Povidone or crospovidone (Kollidone) used in concentration of 2-5% of weight of tablet. Completely insoluble in water.
  Mechanism of Action: Water wicking, swelling and possibly some deformation recovery. Rapidly disperses and swells in water, but does not gel even after prolonged exposure. Greatest rate of swelling compared to other disintegrants. Greater surface area compare to volume ratio than other disintegrants.
- Low-substituted hydroxyl propyl cellulose, which is insoluble in water. Rapidly swells in water. Grades LH-11 and LH-21 exhibit the greatest degree of swelling. Certain grades can also provide some binding properties while retaining disintegration capacity. Recommended concentration 1-5%.
- Cross linked carboxy methyl cellulose sodium (Ac-Di-sol) Croscarmellose sodium
  Mechanism of Action: Wicking due to fibrous structure, swelling with minimal gelling. Effective Concentrations: 1-3% Direct Compression, 2-4% Wet Granulation

PRINCIPLES OF TABLET GRANULATION: [13,14,15,16]

There are three general methods of tablet preparation

1. Direct compression method
2. Dry granulation method
3. Wet granulation method

Wet Granulation	Dry Granulation	Direct Compression
1. Milling and mixing of drugs and excipients	1. Milling and mixing of drugs and excipients	1. Milling and mixing of drugs and excipients
2. Preparation of binder solution	2. Compression into slugs or roll compaction	2. Compression of tablet
3. Wet massing by addition of binder solution or granulating solvent	3. Milling and screening of slugs and compacted powder	-
4. Screening of wet mass	4. Mixing with lubricant and disintegrant	-
5. Drying of the wet granules	5. Compression of tablet	-
6. Screening of dry granules	-	-
7. Blending with lubricant and disintegrant to produce “running powder”	-	-

CONVENTIONAL TECHNIQUE USED IN THE PREPARATION OF IMMEDIATE RELEASE TABLETS: [17,18,19]

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

Tablet Molding:

In this technology, water-soluble ingredients are used so that tablet disintegrate and dissolve rapidly. The powder blend is moistened with a hydro alcoholic solvent and is molded in to tablet using compression pressure lower than used in conventional tablets compression. The solvent is then removed by air-drying. Molded tablets have a porous structure that enhances dissolution. Two problems commonly encountered are mechanical strength and poor taste masking characteristics. Using binding agents such as sucrose, acacia or poly vinyl pyrrolidone can increase the mechanical strength of the tablet. To overcome poor taste masking characteristic Van Scoik incorporated drug containing discrete particles, which were formed by spray congealing a molten mixture of hydrogenated cottonseed oil, sodium bicarbonate, lecithin, polyethylene glycol and active ingredient into a lactose based tablet triturate form.

Direct Compression Method:

In this method, tablets are compressed directly from the mixture of the drug and excipients without any preliminary treatment. The mixture to be compressed must have adequate flow properties and cohere under pressure thus making pretreatment as wet granulation unnecessary. Few drugs can be directly compressed into tablets of acceptable quality. A type of disintegrant and its proportion are of 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

- ✓ The active ingredient and excipients are weighed and mixed.
- ✓ The wet granulate is prepared by adding the liquid binder–adhesive to the powder blend and mixing thoroughly. Examples of binders/adhesives include aqueous preparations of cornstarch, natural gums such as acacia, cellulose derivatives such as methyl cellulose, gelatin, and povidone.
- ✓ Screening the damp mass through a mesh to form pellets or granules.
- ✓ Drying the granulation. A conventional tray-dryer or fluid-bed dryer are most commonly used.
- ✓ After the granules are dried, they are passed through a screen of smaller size than the one used for the wet mass to create granules of uniform size.

Low shear wet granulation processes use very simple mixing equipment, and can take a considerable time to achieve a uniformly mixed state. High shear wet granulation processes use equipment that mixes the powder and liquid at a very fast rate, and thus speeds up the manufacturing process. Fluid bed granulation is a multiple-step wet granulation process performed in the same vessel to pre-heat, granulate, and dry the powders. It is used because it allows close control of the granulation process.

Mass-Extrusion (Mass-Extrusion):

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

By solid dispersions:

When formulating such solid amorphous dispersions into immediate release solid dosage forms for oral administration to a use environment such as the GI tract of an animal such as a human, it is often desirable to maximize the amount of dispersion present in the dosage form. This minimizes the size of the solid dosage form required to achieve the desired dose. Depending on the drug dose, it is often desired that the solid amorphous dispersion comprise at least 30 wt %, preferably at least wt %, and more preferably at least 50 wt % or more of the solid dosage form. Such high drug loadings of dispersion in a solid dosage form minimize the dosage form's size, making it easier for the patient to swallow it and tending to improve patient compliance.

The immediate release dosage forms containing a solid dispersion that enhances the solubility of a “low-solubility drug,” meaning that the drug may be either “substantially water-insoluble,” which means that the drug has a minimum aqueous solubility at physiologically relevant pH (e.g., pH 1-8) of less than 0.01 mg/mL, “sparingly water-soluble,” that is, has an aqueous solubility up to about 1to2 mg/mL, or even low to moderate aqueous- solubility, having an aqueous-solubility from about 1 mg/mL to as high as about 20 to 40 mg/mL.

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

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RESULT AND DISCUSSION

Approximately most of the patients need rapid therapeutic action of drug, resulting in poor compliance with conventional drug therapy which leads to reduced overall therapy effectiveness. 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 improved 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. To fulfill these medical needs, formulators have devoted considerable effort to developing a novel type of tablet dosage form for oral administration, one that disintegrates and dissolves rapidly with enhanced dissolution. 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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