A REVIEW ON IMMEDIATE RELEASE DRUG DELIVERY SYSTEM

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ABSTRACT
Tablet is the most 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 alternative oral dosage forms. There are novel types of dosage forms that act very quickly after administration. The basic approach used in development tablets is the use of superdisintegrants like Cross linked carboxymethylcellulose (Crocarmeliose), Sodium starch glycolate (Primogel, Explotab), Polyvinylpyrrolidone (Polyplasdone) etc. which provide instantaneous disintegration of tablet after administration. The development of immediate release therapy also provides a opportunity for a line extension in the marketplace, A wide range of drugs (e.g., neuroleptics, cardiovascular drugs, analgesics, antihistamines, and drugs can be considered candidates for this dosage form). A new dosage form allows a manufacturer to extend market exclusivity, while offering its patient population a more convenient dosage form or dosing regimen. In this regard, immediate release formulations are similar to many sustained release formulations that are now commonly available.

KEYWORDS: Immediate release, direct compression, super-disintegrants.

INTRODUCTION
Oral route is the most convenient and extensively used for drug 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 suitable for industrial production, improved stability and bioavailability. The concept of immediate release tablets emerged from the desire to provide patient with more conventional means of taking their
medication when emergency treatment is required. Recently, immediate release tablets have gained prominence of being new drug delivery systems. Most immediate release tablets are intended to disintegrate in the stomach, where the pH is acidic. Several orally disintegrating tablet (ODT) technologies based on direct compression. In pharmaceutical formulation includes any formulation in which the rate of release of drug from the formulation is at least 70% (preferably 80%) of active ingredient more preferably within 1.5 hours, and especially within an hour (such as within 30 minutes) of administration. In Formulation of immediate release the commonly Superdisintegrants used are Croscarmellose, sodium, Sodium Starch glycolate and Crospovidone.\textsuperscript{[1, 2, 3]}

**Type and Classes of Tablets**\textsuperscript{[4, 5, 6]}

**A. Oral Tablets for Ingestion**
- 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

**B. Tablets Used in the Oral Cavity**
- Buccal tablets
- Sublingual tablets
- Troches and lozenges
- Dental cones

**C. Tablets Administered by Other Routes**
- Implantation tablets
- Vaginal tablets

**D. Tablets Used to Prepare Solutions**
- Effervescent tablets
DEFINITION

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. Thus, the term excludes formulations which are adapted to provide for “modified”, “controlled”, “sustained”, “prolonged”, “extended” or “delayed” release of drug. Immediate release solid oral dosage forms are classified as either having rapid or slow dissolution rates. Immediate release dosage forms are those for which ≥85% of labelled amount dissolves within 30 min. For immediate release tablets, the only barrier to drug release is simple disintegration or erosion stage, which is generally accomplished in less than one hour1. To enhance dissolution and hence bioavailability of any drug from immediate release tablets, disintegration is one of the important process. Few Super-disintegrant are available commercially as Croscarmellose sodium, Crospovidone and SSG.

Biopharmaceutic Consideration

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

Pharmacokinetics

In this consideration, study has done on absorption, distribution, metabolism 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**[^7]

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

1. Decreased ability of the body to respond reflexive stimuli, cardiac output, and orthostatic hypotension may see in taking antihypertensive like prazosin.
2. Decreased sensitivity of -adrenergic agonist and antagonist.
3. Immunity is less and taken into consideration while administered antibiotics.
4. Altered response to drug therapy-elderly show diminished bronchodilator effect of theophylline shows increased sensitivity to barbiturates.
5. Concomitant illnesses are often present in elderly, which is also taken into consideration, while multiple drug therapy prescribed. Research workers have clinically evaluated drug combination for various classes’ cardiovascular agents, diuretics, antihypertensive etc. for immediate release dosage forms. The combination choice depends on disease state of the patient.

**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

**DIFFICULTIES WITH EXISTING ORAL DOSAGE FORM[^8]**

1. Patient may suffer from tremors therefore they have difficulty to take powder and liquids. In dysphasia physical obstacles and adherence to an oesophagus 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.

CRITERIA FOR IMMEDIATE RELEASE DRUG DELIVERY SYSTEM

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 compatible with taste masking.
- Be portable without fragility concern.
- Have a pleasing mouth feel.
- It should not leave minimal or no residue in the mouth after oral administration.
- Exhibit low sensivity 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.

CANDIDATE FOR IMMEDIATE RELEASE ORAL DOSAGE FORM

Analgesics and Anti-inflammatory Agents
Aloxiprin, auranofin, azapropazone, benorylate, diflunisal, etodolac, fenbufen, fenoprofen calcim, flurbiprofen, ibuprofen, indomethacin, ketoprofen, meclofenamic acid, mefenamicacid, nabumetone, naproxen, oxaprozin, oxyphenbutazone, phenylbutazone, piroxicam, sulindac.

Anthelmintics
Albendazole, bephenium, hydroxynaphthoate, cambendazole, dichlorophen, ivermectin, mebendazole, oxamnique, oxfendazole, oxantel embonate, praziquantel, pyrantel embonate, thiabendazole.

Anti-Arrhythmic Agents
Amiodarone HCl, Disopyramide, flecainide acetate, quinidine sulphate.

Anti-bacterial Agents
Benethamine penicillin, cinoxacin, ciprofloxacin HCl, clarithromycin, clofazimine, cloxacillin, demeclocycline, doxycycline, erythromycin, ethionamide, Imipenem, nalidixic acid, nitrofurantoin, rifampicin, spiramycin, sulphabenzamide, sulphadoxine,
sulphamerazine, sulphacetamide, sulphadiazine, sulphafurazole, sulphamethoxazole, sulphapyridine, tetracycline, trimethoprim.

**Anti-coagulants**
Dicoumarol, dipyridamole, nicoumalone, phenindione.

**Anti-depressants**
Amoxapine, ciclazindol, maprotiline HCl, mianserin HCl, nortriptyline HCl, trazodone HCl, trimipramine maleate.

**Anti-diabetics**
Acetohexamide, chlorpropamide, glibenclamide, gliclazide, glipizide, tolazamide, tolbutamide.

**Anti-epileptics**
Beclamide, carbamazepine, clonazepam, ethotoin, methoin, methsuximide, ethylphenobarbitone, oxcarbazepine, paramethadione, phenacemide, phenoba, rbitone, phenytoin, phensuximide, primidone, sulthiame, valproic acid.

**Anti-fungal Agents**
Amphotericin, butoconazolenitrate, clotrimazole, econazolenitrate, fluconazole, flucytosine, griseofulvin, itraconazole, ketoconazole, miconazole, natamycin, nystatin, sulconazole nitrate, terbinafine HCl, terconazole, tioconazole, undecenoic acid.

**Anti-gout Agents**
Allopurinol, probenecid, sulphinpyrazone.

**Anti-hypertensive Agents**
Amlodipine, carvedilol, benidipine, darodipine, dilitazem HCl, diazoxide, felodipine, guanabenz acetate, indoramin, isradipine, minoxidil, nicardipine HCl, nifedipine, nimodipine, phenoxybenzamine HCl, prazosin HCL, reserpin, terazosin HCl.

**Anti-malarials**
Amodiaquine, chloroquine, chlorproguanil HCl, halofantrine HCl, mefloquine HCl, proguanil HCl, pyrimethamine, quinine sulphate.
Anti-migraine Agents
Dihydroergotamine mesylate, ergotamine tartrate, methysergide maleate, pizotifen maleate, sumatriptan succinate.

Anti-muscarinic Agents
Atropine, benzhexol HCl, biperiden, ethopropazine HCl, hyoscine butyl bromide, hyoscyamine, mepenzolate bromide, orphenadrine, oxyphencyclicmine HCl, tropicamide.

Anti-neoplastic Agents and Immunosuppressants
Aminoglutethimide, amsacrine, azathioprine, busulphan, chlorambucil, cyclosporin, dacarbazine, estramustine, etoposide, lomustine, melphalan, mercaptopurine, methotrexate, mitomycin, mitotane, mitozantrone, procarbazine HCl, tamoxifen citrate, testolactone.

Anti-parkinsonian Agents
Bromocriptine mesylate, lysuride maleate.

Gastro-intestinal Agents
Bisacodyl, cimetidine, cisapride, diphenoxylate HCl, domperidone, famotidine, operamide, mesalazine, nizatidine, omeprazole, ondansetron HCl, ranitidine HCl, sulphasalazine

Histamine H-1-Receptor Antagonists
Acrivastine, astemizole, cinnarizine, cyclizine, cyproheptadine HCl, dimenhydrinate, flunarizine HCl, loratadine, meclozine HCl, oxatomide, terfenadine, triprolidine.

Stimulants
Amphetamine, dexamphetamine, dexfenfluramine, fenfluramine, mazindol, pemoline.

EXCIPIENTS
Excipients balance the properties of the actives in Immediate release dosage forms. This demands a thorough understanding of the chemistry of these excipients to prevent interaction with the actives. Determining the cost of these ingredients is another issue that needs to be addressed by formulators. 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 efficacy. Excipients are general and can be used for a broad range of actives, except some actives that require masking agents.

**BULKING AGENTS**

Bulking agents are significant in the formulation of fast-melting tablets. The material contributes functions of a diluents, filler and cost reducer. Bulking agents improve the textural characteristics that in turn enhance the disintegration in the mouth, besides; adding bulk also reduces the concentration of the active in the composition. The recommended bulking agents for this delivery system should be more sugar-based such as mannitol, polydextrose, lactitol, DCL (direct compressible lactose) and starch hydrolystate for higher aqueous solubility and good sensory perception. Mannitol in particular has high 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.

**LUBRICANTS**

Lubricants, though not essential 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.

**SUPER DISINTEGRANTS**

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

**ADVANTAGES**

1. Effective in lower concentrations
2. Less effect on compressibility and flowability
3. More effective intragranularly

Some super disintegrants are

1) 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

2) Cross-linked Povidone (crosppovidone) (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 to volume ratio than other disintegrants.

3) 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%

4) Cross linked carboxy methyl cellulose sodium (i.e. 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.

Conventional Technique Used In the Preparation of Immediate Release Tablets\[^{[10,11,12]}\]

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

1) Tablet Molding

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

2) Methods for tablet preparation

A. Granulation method.
   a. Wet granulation.
   b. Dry granulation.
B. Direct compression method

A. 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.

B. Direct Compression Method

The term “direct compression” is defined as the process by which tablets are compressed directly from powder mixture of API and suitable excipients. No pretreatment of the powder blend by wet or dry granulation procedure is required. Amongst the techniques used to prepare tablets, direct compression is the most advanced technology. It involves only blending and compression, thus offering advantage particularly in terms of speedy production, as it requires fewer unit operations, less machinery, reduced number of personnel and considerably less processing time along with increased product stability.

Procedure

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

Step 2: The wet granulate is prepared by adding the liquid binder–adhesive to the powder blend and mixing thoroughly. Examples of binders/adhesives include aqueous preparations of cornstarch, natural gums such as acacia, cellulose derivatives such as methyl cellulose, gelatin, and povidone.

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

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

Step 5: After the granules are dried, they are passed through a screen of smaller size than the one used for the wet mass to create granules of uniform size.

Table 1: Steps involved in this process:

<table>
<thead>
<tr>
<th>Wet Granulation</th>
<th>Dry Granulation</th>
<th>Direct compression</th>
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<tbody>
<tr>
<td>Blending</td>
<td>Blending</td>
<td>Blending</td>
</tr>
<tr>
<td>Wet massing and screening</td>
<td>Slugging/roller compression</td>
<td>-</td>
</tr>
<tr>
<td>Drying</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Dry screening</td>
<td>Screening</td>
<td>-</td>
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<tr>
<td>Blending (with lubrication)</td>
<td>Blending (with lubrication)</td>
<td>Blending(with lubrication)</td>
</tr>
<tr>
<td>Compaction</td>
<td>Compaction</td>
<td>Compaction</td>
</tr>
</tbody>
</table>
4) 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.

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

Drug-excipient compatibility studies
The proper design and the formulation of a dosage form require consideration of the physical, chemical and biological characteristics of the drug and excipients used in fabricating the product. The drug and excipients must be compatible with one another to produce a product i.e. stable, efficacious, attractive, easy to administer and safe. The compatibility studies provide the frame work for the drugs combination with the excipients in the fabrication of the dosage form. The study was carried out to establish that the therapeutically active drug has not undergone any changes, after it has been subjected to processing steps during formulation of tablets. Compatibility studies are carried out by mixing definite properties of drug and excipient and kept in glass vials, which is stored at 55°C for one month.

EVALUATION OF IMMEDIATE RELEASE TABLETS[16]
The blend is evaluated by following tests.
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 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.

\[ \tan = \frac{h}{r} \]

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

![Image of angle of repose measurement](image)

**Figure1: Measurement of angle of repose (Fixed Funnel method).**

2. **Bulk density**

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

\[ \text{Bulk Density (BD)} = \frac{\text{Weight of granules (m)}}{\text{untapped volume of granules (v)}} \]

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 graduated cylinder and height is measured. Then cylinder was allowed to 100tap 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.

\[ \text{Tapped Density (TD)} = \frac{\text{Weight of granules (m)}}{\text{tapped volume of granules (v)}} \]
Here; m = weight of powder or granules (gm)
\( v = \text{Tapped Volume (cm.3)} \)

**Compressibility Index**

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

4. **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.

\[
\text{Carr’s Index (\%)} = \frac{[(\text{TBD} - \text{LBD}) \times 100]}{\text{TBD}}
\]

5. **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.

\[
\text{Hausner’s Ratio} = \frac{\text{Tapped density}}{\text{Poured density}}
\]

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

**Compression**

Mixed Blends is compressed by direct compression method using Cadmach single punch machine. Caput punches and die (8 mm.) were used in this study.

**In-vitro Evaluation of the prepared tablets**\(^{13, 14, 15}\)

These tests are as following

1. Appearance
2. Thickness
3. Hardness
4. Weight variation
5. Friability
6. Disintegration
7. Drug content
8. In vitro Dissolution
9. Stability studies
1. Appearance
The general appearance of tablet is its visual identity and all over elegance, shape, color, surface textures. These all parameters are essential for consumer acceptance.

2. Thickness
The thickness of the tablets was determined by using vernier calipers. Randomly 10 tablets selected were used for determination of thickness that expressed in Mean± SD and unit is mm.

3. Hardness
The hardness of tablet is an indication of its strength against resistance of tablets to capping, abrasion or breakage under conditions of storage, transportation and handling before usage. Measuring the force required to break the tablet across tests it. Hardness of 10 tablets (randomly) from whole tablet batch was determined by Monsanto hardness tester. Hardness measured in kg/cm².

4. Weight variation
The weight variation test is carried out in order to ensure uniformity in the weight of tablets in a batch. The total weight of 20 tablets randomly from whole batch was determined and the average was calculated. The individual weights of the tablets were also determined accurately and the weight variation was calculated.

5. Friability test
Friability is the loss of weight of tablet in the container due to removal of fine particles from the surface during transportation or handling. Roche friabilator was employed for finding the friability of the tablets. 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 0.65 g take a sample of 10 whole tablets. Roche friabilator is rotated at 25rpm for 4 minutes for 100 rounds. The tablets were dedusted and weighed again. The percentage of weight loss was calculated using the formula

\[ \%f = \frac{W0-W1}{W0} \times 100 \]

\( \%f \) = Percentage friability

W0 = Initial weight (Before test)

W1 = Final weight (After test)
6. **Disintegration test**

The USP device to rest disintegration was six glass tubes that are “3 long, open at the top, and held against 10” screen at the bottom end of the basket rack assembly. One tablet is placed in each tube and the basket rack is poisoned in 1 liter beaker of distilled water at 37± 2 °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.

7. **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.

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±10°C. The tablets are kept in the cylindrical basket or directly placed in medium with paddle then rotated at 100 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 spectrophotometrically 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.

**Dissolution Profile**[^17]

The compositions of the present invention preferably are immediate release compositions from which about 50% of the micronized drug is dissolved in vitro within about 15 minutes, more preferably at least about 80% of the drug is dissolved in vitro within about 30 minutes, and still more preferably at least about 90% of the e is dissolved in vitro within about 45 minutes using 1% sodium dodecyl sulfate (SDS) in water as the dissolution medium at 37° C.
9. Stability study

Stability is defined as the ability of a particular drug or dosage form in a specific container to remain within its physical, chemical, therapeutic, and toxicological specifications. Drug decomposition or degradation occurs during storage, because of chemical alteration of the active ingredients or due to product instability, lowering 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 invitro 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

<table>
<thead>
<tr>
<th>Study Storage condition</th>
<th>Minimum time period covered by data at submission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long term</td>
<td>25°C ± 2°C/60% RH ± 5% RH or 30°C ± 2°C/65% RH ± 5% RH 12 months</td>
</tr>
<tr>
<td>Intermediate</td>
<td>30°C ± 2°C/65% RH ± 5% RH 6 months</td>
</tr>
<tr>
<td>Accelerated</td>
<td>40°C ± 2°C/75% RH ± 5% RH 6 months</td>
</tr>
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</table>

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

Due to the constraints of the current technologies there is a 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.
REFERENCES