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IMMEDIATE RELEASE DRUG DELIVERY SYSTEM- A REVIEW

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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 (Croscarmellose), Sodium starch glycolate (Primogel, Explotab), Polyvinylpyrrolidone (Polyplasdone) etc. which provide instantaneous disintegration of tablet after administration. Immediate release liquid dosage forms and parenteral dosage form have also been introduced for treating patients. Dosage form can be suspensions with typical dispersion agents like hydroxypropylmethylcellulose, (dioctylsulfosuccinate) etc. 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 drugs can be considered candidates for this dosage form. As a drug entity nears the end of its patent life, it is common for pharmaceutical manufacturers to develop a given drug entity in a new and improved dosage form.

KEY WORDS

Immediate release drug delivery system, Onset of action and Superdisintegrants.

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INTRODUCTION

Oral Solid Dosage Forms

In a country like India with an increase in population, the demand for health care services is also increasing. With changing lifestyles and so-called “fast culture” good health is almost deprived part. In this tremendous speed of life, the health, as defined by World Health Organization (WHO) is difficult to attain. With the up gradation

of lifestyle, the concepts and severity of illness, diseases and disorders are also changing. The major challenge faced by healthcare professionals in this view is that of gradation of the available drug delivery systems. The ultimate goal of any drug delivery system is effective disease/disorder management, minimum side effects and greater patient compliance in a cost effective manner. The drug therapeutic indices could be maximized while indices of adverse reactions or side effects could be minimized by regulating the drug release in body in a well-defined controlled manner. This would eliminate the haphazard and uncontrolled blood plasma profiles of drugs usually associated with conventional dosage forms¹. Tablets are solid medications that are compacted into small, formed shapes. Tablets are usually taken by the mouth for oral administration. Tablets consist of several components. These components work together to ensure that the tablet is properly digested in the body, is easy to swallow, has flavorings or sweeteners for taste, and controls the timed release of the drug to produce the desired effect. All of the ingredients except the active drug are called inactive or inert ingredients.

Classification and Types of Tablets¹⁻⁶

A. Oral Tablets for Ingestion

1. Compressed tablets
2. Multiple compressed tablets
3. Layered tablets
4. Compression-coated tablets
5. Repeat-action tablets
6. Delayed-action and enteric-coated tablets
7. Sugar and chocolate-coated tablets
8. Film coated tablets
9. Chewable tablets

B. Tablets Used in the Oral Cavity

1. Buccal tablets
2. Sublingual tablets
3. Troches and lozenges
4. Dental cones

C. Tablets Administered by Other Routes

1. Implantation tablets
2. Vaginal tablets

D. Tablets Used to Prepare Solutions

1. Effervescent tablets
2. Dispensing tablets
3. Hypodermic tablets
4. Tablet triturates

DEFINITION^{1,7}

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. In this context, the term “release” 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.

Various considerations for Immediate release tablets

Biopharmaceutical Consideration

When new drug delivery system put on, it is must

that to consider Biopharmaceutical factor like metabolism and excretion.

Pharmacokinetics

In this consideration, study has done on absorption, distribution, metabolism and excretion.

Pharmacodynamic

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.

DIFFICULTIES WITH EXISTING ORAL DOSAGE FORM^{5, 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 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. Buccal and sublingual formation may cause irritation to oral mucosa, so patients refused to use such medications.
4. Cost of products is main factor as parenteral formulations are most costly and discomfort.

DESIRED CRITERIA FOR IMMEDIATE RELEASE DRUG DELIVERY SYSTEM^{7, 8}

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

1. In the case of liquid dosage form it should be compatible with taste masking.
2. It should not leave minimal or no residue in the mouth after oral administration.
3. Exhibit low sensitivity to environmental condition as humidity and temperature.

4. Be manufactured using conventional processing and packaging equipment at low cost.
5. Rapid dissolution and absorption of drug, which may produce rapid onset of action.

POTENTIAL CANDIDATE FOR IMMEDIATE RELEASE ORAL DOSAGE FORM⁷

Analgesics and Anti-inflammatory Agents

Auranofin, Azapropazone, Diflunisal, Fenbufen, Fenoprofen Calcim, Ibuprofen, Indomethacin, Ketoprofen, Meclofenamic Acid.

Anthelmintics

Albendazole, Dichlorophen, Mebendazole, Oxamniquine, Oxfendazole, Oxantel Embonate, Embonate, Thiabendazole.

Anti-Arrhythmic Agents

Amiodarone Hcl, Disopyramide, Flecainide Acetate.

Anti-bacterial Agents

Benethamine Penicillin, Cinoxacin, Ciprofloxacin Hcl, Clarithromycin.

Anti-coagulants

Dicoumarol, Dipyridamole.

Anti-coagulants

Dicoumarol, Dipyridamole.

Anti-fungal Agents

Amphotericin, Butoconazolenitrate, Clotrimazole, Econazolenitrate.

Anti-gout Agents

Allopurinol, Probenecid, Sulphinpyrazone.

Anti-hypertensive Agents

Amlodipine, Carvedilol, Benidipine, Darodipine, Dilitazem Hcl.

Anti-migraine Agents

Dihydroergotamine Mesylate, Succinate.

Anti-muscarinic Agents

Atropine, Benzhexol Hcl, Biperiden, Ethopropazine Hcl.

Anti-neoplastic Agents and Immunosuppressants

Aminoglutethimide, Amsacrine Chlorambucil, Cyclosporin, Dacarbazine, Estramustine.

Anti-protazoal Agents

Metronidazole, Nimorazole, Nitrofurazone, Omidazole, Tinidazole.

Anti-thyroid Agents

Carbimazole and Propylthiouracil.

Anxiolytic, Sedatives, Hypnotics and Neuroleptics

Alprazolam, Amylobarbitone, Barbitone.

Cardiac Inotropic Agents

Amrinone, Digoxin, Digoxin.

Corticosteroids

Beclomethasone, Betamethasone, Budesonide, Cortisone Acetate.

Diuretics

Acetazolamide, amiloride, bendrofluazide, bumetanide, chlorothiazide, chlorthalidone.

Enzymes

All Enzymes.

Anti-parkinsonian Agents

Bromocriptin mesylate, lysuride maleate.

Gastro-intestinal Agents

Bisacodyl, cimetidine, cisapride, diphenoxylate Hcl, famotidine.

Histamine H₁-Receptor Antagonists

Acrivastine, astemizole, cinnarizine, cyclizine.

Lipid Regulating Agents

Bezafibrate, Clofibrate, Fenofibrate, Gemfibrozil, Probucol.

Local Anaesthetics

Lidocaine.

Neuro-muscular Agents

Pyridostigmine.

Nitrates and other Anti-anginal Agents

Amyl Nitrate, Glyceryl trinitrate, Isosorbide Dinitrate.

Sex Hormones

Clomiphene citrate, danazol, ethinylloestradiol, medroxyprogesterone acetate.

Advantages of Immediate Release Drug Delivery System^{9,10}

An immediate release pharmaceutical preparation offers:

1. Improved stability and bioavailability.
2. Improved compliance/added convenience
3. Quick onset of action.
4. Suitable for controlled/sustained release actives
5. Allows high drug loading.
6. Suitable for industrial production.

Disadvantages of Immediate Release Tablets

1. Rapid drug therapy intervention is not possible.

2. Sometimes may require more frequency of administration.

3. Dose dumping may occur.

EXCIPIENTS USED IN IMMEDIATE RELEASE DRUG DELIVERY SYSTEM⁵⁻⁹

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 (Figure No.1).

SUPER DISINTEGRANTS^{7,8}

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

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

Commonly used Super disintegrates are

Sodium Starch Glycolate (Explotab, primogel) used in concentration of 2-8 % and 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. Water wicking.

Cross-linked Povidone (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 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 (i.e. Ac-Di-sol) Croscarmellosesodium

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

1. Tablet molding technique
2. Direct compression technique
3. Wet granulation technique
4. Mass extrusion technique

Tablet Molding¹⁰

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.

Direct Compression⁴⁻⁷

The term direct compression is used to define the process by which tablets are compressed directly from powder blends of the active ingredient and suitable excipients which will flow uniformly into a die cavity and form into a firm compact.

Procedure

Step 1: Premilling of formulation components.

Step 2: Mixing of the therapeutic agent with the powdered excipients (including the lubricant).

Step 3: Compression of the mixed powders into tablets.

Advantages

1. Direct compression is more suitable for moisture and heat sensitive drugs, since it eliminates wetting and drying steps and increases the stability of active ingredients by reducing detrimental effects.
2. Changes in dissolution profiles are less likely to occur in tablets made by direct compression on storage than in those made from granulations.

3. It is suitable for low dose drugs.
4. Saving equipment, space and personnel.
5. Fewer formulation excipients.
6. Better physical and chemical stability.
7. Superior tablet disintegration.
8. Shorter "time to market".

Disadvantages

1. Direct compression is more prone to segregation due to the difference in density of the API and excipients.
2. The dry state of the material during mixing may induce static charge and lead to segregation.
3. Most of the directly compressible materials can accommodate only 30-40 % of the poorly compressible active ingredients like acetaminophen.

Granulation

Granulation may be defined as a size enlargement process which converts small particles into physically stronger & larger agglomerates. The objective of granulation is to improve powder flow and handling, decrease dustiness, and prevent segregation of the constituents of the product.

Granulation method can be broadly classified into two types

1. Wet granulation and
2. Dry granulation

Wet granulation^{8,10}

Wet granulation is a commonly used unit operation in the pharmaceutical industry. Wet granulation is often carried out utilizing a high-shear mixer. The high-shear granulation process is a rapid process which is susceptible for over-wetting. Thus, the liquid amount added is critical and the optimal amount is affected by the properties of the raw materials. Power consumption of the impeller motor and the impeller torque have been applied to monitor the rheological properties of the wet mass during agglomeration and, thereby, have been used to determine the end-point of water addition.

Important steps involved in wet granulation

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

Step 2: A wet granulate is prepared by adding the liquid binder to the powder blend and mixing thoroughly.

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

Step 4: Drying the granulation.

Step 5: After the granules are dried, they are passed through a screen of smaller size than the one used earlier.

Step 6: After granulation a final lubrication step is used to ensure that the tableting blend does not stick to the equipment during the tableting process.

Limitation of wet granulation

1. It requires a number of pieces of expensive equipment.
2. Because of the large number of processing steps, it requires a large area with temperature and humidity control.
3. There is a greater possibility of cross-contamination than with the direct-compression method.
4. The greatest disadvantage of wet granulation is its cost. It is an expensive process because of labor, time, equipment, energy and space requirements.
5. Stability may be a major concern for moisture sensitive or thermolabile drugs.

Advantages

1. Reduced segregation of formulation components during storage and/or processing, leading to reduced intra- and inter batch variability.
2. Useful technique for the manufacture of tablets containing low concentrations of therapeutic agent.
3. Employs conventional excipients and therefore is not dependent on the inclusion of special grades of excipient.
4. Most manufacturing plants are built around wet granulation tablet manufacture.
5. Tablets produced by wet granulation are amendable to post processing unit operations, e.g. tablet-coating techniques.

Dry Granulation^{10,11,12}

Dry granulation processes create granules by light compaction of the powder blend under low pressures. The compacts so-formed are broken up gently to produce granules (agglomerates). This process is often used when the product to be granulated is sensitive to moisture and heat. Dry granulation can be conducted on a tablet press using slugging tooling or on a roll press called a roller compactor. Dry granulation equipment offers a wide range of pressures to attain proper densification and granule formation. Dry granulation requires drugs or excipients with cohesive properties, and a 'dry binder' may need to be added to the formulation to facilitate the formation of granules. At last powdered lubricants are added.

Advantages

1. Both roller compaction and slugging require conventional grades of excipients.
2. These methods are not generally associated with alterations in drug morphology during processing.
3. No heat or solvents are required.
4. The main advantages of dry granulation or slugging are that it uses less equipments and space. It eliminates the need for binder solution, heavy mixing equipment and the costly and time consuming drying step required for wet granulation. Slugging can be used for advantages in the following situations:
 - For moisture sensitive material
 - For heat sensitive material.

Disadvantages

1. Specialist equipment is required for granulation by roller compaction.
2. Segregation of components may occur post mixing.
3. There may be issues regarding powder flow.
4. The final tablets produced by dry granulation tend to be softer than those produced by wet granulation, rendering them more difficult to process using post-tableting techniques, e.g. film coating.
5. Slugging and roller compaction may lead to the generation of considerable dust.

6. It requires a specialized heavy duty tablet press to form slug.

Immediate release solid dosage forms prepared by solid dispersions⁷

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.

EVALUATION PARAMETERS OF IMMEDIATE RELEASE TABLETS¹¹⁻¹⁵

Compatibility studies⁷

The proper design and formulation of a dosage form requires consideration of the physical, chemical and biological characteristic of the ingredients used in fabricating the formulation i.e. the drug and all the excipient used in the formulation. The drug and the excipients should be compatible with one another to produce stable, efficacious, attractive and easy to administer and safe dosage form.

Evaluation of Blend⁹

The prepared blend is evaluated by following tests.

1. Angle of repose
2. Bulk density
3. Tapped density
4. Carr's index and
5. Hauser's ratio.

Evaluation of Tablets⁷

The tablets are subjected to the following quality control tests:

1. Weight variation
2. Friability
3. Hardness
4. Disintegration

5. Wetting Time
6. Water absorption Ratio
7. Taste / Mouth feel
8. *In vitro* Dissolution
9. Stability studies.

Dosage of Pharmaceutical Composition

The pharmaceutical compositions contains micronized drug in an amount of about 10mg to about 1000 mg. Preferably, the pharmaceutical compositions comprise micronized drug in an amount of about 20 mg to about 400 mg, more preferably from about 25 mg to about 200 mg, and still more preferably from about 25 mg to about 150 mg. It also has been found that then pharmaceutical compositions of the present invention provide a daily dosage of eplerenone sufficient to cause an average decrease in diastolic blood pressure in humans over an interval of about 12 to 24 hours, preferably about 24 hours, after ingestion of the composition of at least about 5%.

Unit Dosages

Dosage unit forms of the pharmaceutical compositions can typically contain, for example, 10, 20, 25, 37.5, 50, 75, 100, 125, 150, 175, 200, 250, 300, 350 or 400 mg of drug. Preferred dosage unit forms contain about 25, 50, 100, or 150 mg of micronized drug. The dosage unit form can be selected to accommodate the desired frequency of administration used to achieve the specified daily dosage. The amount of the unit dosage form of the pharmaceutical composition that is administered and the dosage regimen for treating the condition or disorder depends on a variety of factors, including the age, weight, sex and medical condition of the subject, the severity of the condition or disorder, the route and frequency of administration, and thus can vary widely, as is well known.

Form of Pharmaceutical Compositions

The pharmaceutical compositions of the present invention comprise micronized drug in association with one or more non-toxic, pharmaceutically-acceptable carriers, excipients and/or adjuvants (collectively referred to herein as "carrier materials"). The carrier materials are acceptable in the sense of being compatible with the other

ingredients of the composition and are not deleterious to the recipient. The pharmaceutical compositions of the present invention can be adapted for administration any suitable route by selection of appropriate carrier materials and a dosage of eplerenone effective for the treatment intended. For example, these compositions can be prepared in a form suitable for administration orally, intravascularly, intraperitoneally, subcutaneously, intramuscularly (IM) or rectally. Accordingly, the carrier material employed can be a solid or a liquid, or both, and is preferably formulated with the compound as a unit-dose composition, for example, a tablet, which can contain from about 1% to about 95%, preferably about 10% to about 75%, more preferably about 20% to about 60%, and still more preferably about 20% to about 40%, by weight of micronized eplerenone.

Oral Administration

For oral administration, the pharmaceutical composition can contain a desired amount of micronized drug and be in the form of, for example, a tablet, a hard or soft capsule, a lozenge, a cachet, a dispensable powder, granules, a suspension, an elixir, a liquid, or any other form reasonably adapted for oral administration.

Carrier Materials

As noted above, for therapeutic purposes, the pharmaceutical compositions of the present invention comprise micronized drug in a desired amount in combination with one or more pharmaceutically-acceptable carrier materials appropriate to the indicated route of administration. Oral dosage forms of the pharmaceutical compositions of the present invention preferably comprise micronized drug in a desired amount admixed with one or more carrier materials selected from the group consisting of diluents, disintegrants, binding agents and adhesives, wetting agents, lubricants, anti-adherent agents and/or other carrier materials.

Disintegrants

The pharmaceutical compositions of the present invention optionally can comprise one or more

disintegrants as a carrier material, particularly for tablet formulations. Suitable disintegrants can include, either individually or in combination, such disintegrants as starches; sodium starch glycolate; clays (such as Veegum™ HV); celluloses (such as purified cellulose, methylcellulose and sodium carboxymethylcellulose, and carboxy methyl - cellulose); alginates; pregelatinized corn starches (such as National™ 1551 and National™ 1550); croscopovidone USP NF; gums (such as agar, guar, locust bean, Karaya™, pectin, and tragacanth). Disintegrants can be added at any suitable step during the preparation of the pharmaceutical composition, particularly prior to granulation or during the lubrication step prior to compression. The present pharmaceutical compositions comprise one or more disintegrants in the range of about 0.5% to about 30%, preferably about 1% to about 10%, and more preferably about 2% to about 6%, of the total weight of the composition. Croscarmellose sodium is a preferred disintegrant for tablet formulations, preferably in the range of about 1% to about 10%, preferably about 2% to about 6%, and more preferably about 5%, by weight of the composition.

Wetting agents

Eplerenone, even micronized eplerenone, is largely insoluble in aqueous solution. Accordingly, the pharmaceutical compositions of the present invention optionally can comprise one or more wetting agents as a carrier material, particularly for tablet formulations. Such wetting agents preferably maintain eplerenone in solution and improve the bioavailability of the pharmaceutical composition. Suitable wetting agents include, individually or in combination, such wetting agents as oleic acid; glyceryl monostearate; sorbitan monooleate; sorbitan monolaurate; triethanol amineoleate; polyoxyethylene sorbitan mono-oleate; polyoxyethylene sorbitan monolaurate; sodium oleate; and sodium lauryl sulfate. Wetting agents that are anionic surfactants are preferred.

Lubricants

The pharmaceutical compositions optionally comprise one or more lubricants and/or glidants as a carrier material. Suitable lubricants and/or glidants

include, either individually or in combination, such lubricants and/or glidants as glycerylbehenate (Compritol™ 888); metallic stearates (e.g., talc; waxes; Stearowet™; boric acid; sodium benzoate and sodium acetate; sodium chloride; DL-Leucine; polyethylene glycols (e.g., Carbowax™ 4000 and Carbowax™ 6000); sodium oleate; sodium benzoate; sodium acetate; sodium lauryl sulfate; sodium stearyl fumarate (Pruv™); and magnesium lauryl sulfate.

Dissolution Profile

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 eplerenone is dissolved in vitro within about 45 minutes using 1% sodium dodecyl sulfate (SDS) in water as the dissolution medium at 37° C. in the dissolution assay discussed hereinafter. More preferably, 0.1N Hcl in water at 37° C. is the in vitro dissolution medium in that assay, and about 50% of the micronized drug is dissolved in about 20 minutes, about 80% is dissolved at about 45 minutes and greater than about 90% is dissolved in about 90 minutes. More preferably, about 50% of the micronized eplerenone is dissolved in about 15 minutes; about 80% is dissolved at about 30 minutes and about 90% or more is dissolved in about 45 minutes.

magnesium, calcium and sodium stearates); stearic acid; hydrogenated vegetable oils (e.g., Sterotex™);

Disintegration Profile

Carrier materials for immediate release compositions preferably are selected to provide a disintegration time less than about 30 minutes, preferably about 20 minutes or less, more preferably about 18 minutes or less, and still more preferably about 14 minutes or less.

Hardness

For tablet formulations, the pharmaceutical composition in an amount sufficient to make a uniform batch of tablets is subjected to tableting in a conventional production scale tableting machine at normal compression pressure (for example, about 1kN to about 50 kN). Any tablet hardness convenient with respect to handling, manufacture, storage and ingestion may be employed. Hardness in the range of about 3.5 kP to about 22 kP is typically acceptable, with about 3.5 kP to about 9 kP preferred for 25 mg tablets, about 5 kP to about 13 kP preferred for 50

mg tablets, and about 8 kP to about 22 kP preferred for 100 mg tablets. The mixture, however, is not be compressed to such a degree that there is subsequent difficulty in achieving hydration when exposed to gastric fluid.

Friability

For tablet formulations, tablet friability preferably is less than about 0.8%, more preferably less than 0.4%.

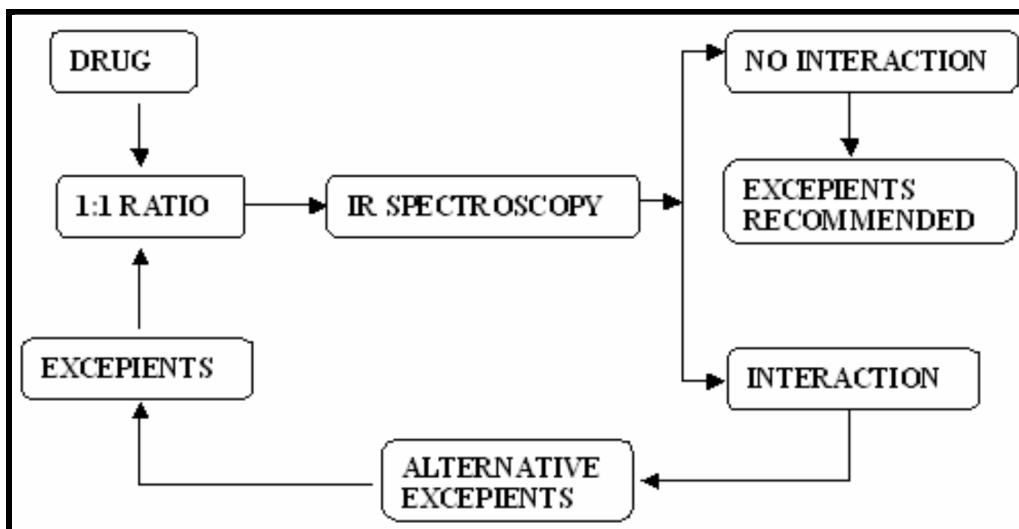


Figure No.1: Schematic representation of compatibility studies

CONCLUSION

There is a clear opportunity for new enhanced oral products arising within this market segment. This proprietary technology is applicable to wide range of therapeutic agents including generics, thereby adding value, i.e. 'supergenerics' for veterinary or human application. Approximately one-third of the patients need quick 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.

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CONFLICT OF INTEREST

We declare that we have no conflict of interest.

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