Available online at http://jddtonline.info

REVIEW ARTICLE

IMMEDIATE RELEASE TABLET OF ANTIHYPERTENSIVE DRUG OLMESARTAN MEDOXOMILE

Mayur V. Mahida*,M. M. Gupta[1]

Department of Pharmaceutics, Jaipur College of Pharmacy, Jaipur (Rajasthan) India

Corresponding Author's Email id: mahidamayur2@gmail.com

ABSTRACT:

Olmesartan medoxomile blocks the vasoconstrictor and aldosterone-secreting effects of angiotensin II by selectively binding to the AT1 angiotensin II receptor. ACE inhibitor is used in treatment of hypertension. Olmesartan medoxomile tablet have been prepared by wet granulation method and also by direct compression. Effect of various fillers and disintegrants were also explored. Microcrystalline cellulose, lactose monohydrate, were used in wet granulation. In order to obtain acceptable product several trials were conducted.And ten different formulations were prepared. Various pharmacopoeial evaluations of the formulations were conducted including weight variation, hardness, disintegrationtime, friability and *in-vitro* dissolution. Final selection of formulation was done based on pharmaceutical equivalence of development formulation to that of marketed one.

Keywords: Immediate release tablet, Superdisintegrants, lactose monohydrate, hypertension.

INTRODUCTION:

The oral route of drug administration is the most popular and successfully used for conventional delivery of drugs. It offers the advantages of convenience, ease of administration, greater flexibility in dosage form design, ease of production, and low cost. The parenteral route of administration is important in case of emergencies, while the topical route of drug administration recently employed to deliver drug to the specific part of the body for systemic effect. It is probable that almost 90% of all the drugs are administered by oral route. Tablets are solid preparations each containing a single dose of one or more active substances and usually obtained by compressing uniform volumes of particles. Tablets are intended for oral administration. Some are swallowed whole, some after being chewed, some are dissolved or dispersed in water before being administered and some are retained in the mouth where the active substance is liberated. The particles consist of one or more active substances with or without excipients such as diluents, binders, disintegrating agents, glidants, lubricants, substances capable of modifying the behavior of the preparation in the digestive tract coloring matter authorized by the competent authority and flavoring substances.The dosage form available for oral administrations are solutions, suspensions,powders, tablets and capsules. The physical state of most of the drugs being solid,they are administered in solid dosage form.

The drugs administered by oral route are versatile, flexible in dosage strength, relatively stable, present lesser problem in formulation and packaging and are convenient to manufacturer, store, handle and use. Solid dosage forms provide best protection to drugs against temperature, light, oxygen and stress during transportation.

Advantages of tablets

- They are unit dosage form, and they offer the capabilities of all oral dosage forms for the dose precision and the least content variability during dosing
- Accuracy and uniformity of drug content
- Optimal drug dissolution and hence, availability from the dosage form for absorption consistent with intended use (i.e., immediate or extended release).
- Usually taken orally, but can be administered sublingually, rectally or intravaginally.
- Their cost is lowest of all oral dosage forms
- They are the most compact of all oral dosage forms
- They are in general the easier and cheaper to package and ship as compare to other oral dosage forms
- Product identification is simple and cheap, requiring no additional processing steps when employing an embossed or monogrammed punch face
- They are ease to administer, does not require a specialist
- They are better suited to large-scale production than other unit oral forms
- They have the better properties of chemical, mechanical and microbiological stability

Disadvantages [2]

- Some drugs resist compression, due to their amorphous nature or low-density
- Drugs having bitter taste, objectionable odor or drugs that are sensitive to oxygen may require encapsulation or coating of tablet
- Bioavailability problems.
- Chance of GI irritation caused by locally high concentrations medicament.
- Difficulty in swallowing tablets in a small proportion of people and so size and shape become important considerations.
- Slow onset of action as compared to parenterals and solutions

Types and Classes of Tablets [1-3]

Tablets are classified by their route of administration or functions

1) Oral tablets for ingestion

- Compressed tablets or standard compressed tablets
- Multiple compressed tablets (MCT)

a) Layered tablets

b) Compression coated tablets

- Repeat action tablets
- Sustained release or modified release tablets
- Delayed action or enteric-coated tablets
- Film coated tablets
- Chewable tablets

2) Tablets used in oral cavity

- Buccal tablets
- Sublingual tablets
- Troches and lozenges
- Dental cones

3) Tablets administered by other routes

- Implantation tablets
- Vaginal tablets

4) Tablets used to prepare solutions

- Effervescent tablets
- Dispersible tablets
- Hypodermic tablets
- Tablet triturates

❖ **The pharmaceutical tablet dosage form**

Ideal properties of tablets and basic consideration [4-6]

Tablets are the most popular solid dosage forms used nowadays, due to ease of manufacture and administration for the patient. About two-thirds of all prescriptions are dispensed as solid dosage forms, and half of these are compressed tablets. Tablet drug delivery system can range from relatively simple immediate-release formulations to complex extended or modified-release dosage forms. A tablet is a mixture of active pharmaceutical ingredient (API) and excipients, usually in powder form, pressed or compacted into a solid. The excipients include binders, lubricants, glidants (flowaids), disintegrants, sweeteners or flavors and pigments. A coating may be applied to hide the taste of the tablet's components, to make the tablet smoother and easier to swallow, and to make it more resistant to the environment, extending its shelf life.Tablets are often stamped with symbols, letters, and numbers, which enable them to be identified. Size of tablet is from a few millimeters to centimeter. Some tablets are in the shape of capsules, and are called "caplets". Excipients are critical to the design of the delivery system and play a major role in determining its quality and performance. They may be selected to enhance stability (antioxidants, UV absorbers), optimize or modify drug release (disintegrants,hydrophilic polymers, wetting agents, biodegradable polymers), provide essential manufacturing technology functions (binders, glidants, lubricants), enhance patient acceptance (flavors), or aid in product identification (colorants). Thus a tablet formulation is not a random combination of ingredients, but rather a carefully throughout, rational formulation designed to satisfy the above criteria. The objectives of the design and manufacture of the compressed tablet is to deliver orally the correct amount of drug in the proper form, at or over the proper time and in the desired location. Beside the physical and chemical properties of medicinal agents formulated as a tablet, it should posses following characteristics.

- Should be an elegant product having its own identity, while being free of defects such as chips, cracks, discoloration, contamination and the like
- Should have the strength to withstand rigors of mechanical shocks encountered in its production, packaging, shipping and dispensing
- Should have the chemical and physical stability to maintain its physical/chemical attributes over time
- It must be able to release the medicinal agents in the body in a predictable and reproducible manner
- Must have suitable chemical stability over a time so as not to allow alteration of the medicinal agents

Tablet Manufacturing [7,8]

The manufacturing of oral solid dosage forms such as tablets is a complex multi-stage process under which the starting materials change their physical characteristics a number of times before the final dosage form is produced. Traditionally, tablets have been made by granulation. Both wet granulation and dry granulation or direct compression is used.

Following are the various unit processes which are involved in making tablets

1. Dispensing
2. Sizing
3. Powder blending
4. Granulation
5. Drying
6. Tablet compression
7. Packaging

Various factors associated with these processes can seriously affect content uniformity, bioavailability or stability.

1. Dispensing (weighing and measuring)

Dispensing is the first step in any pharmaceutical manufacturing process. It is one of the most critical steps in pharmaceutical manufacturing; as during this step, the weight of each ingredient in the mixture is determined according to dose. Dispensing may be done manually by hand scooping from primary containers and weighing each ingredient by hand on a weigh scale, manual weighing with material lifting assistance like vacuum transfer and bag lifters, manual or assisted transfer with automated weighing on weigh table, manual or assisted filling of loss-in weight dispensing system, automated dispensaries with mechanical devices such as vacuum loading system and screw feed system.

2. Sizing

Sizing is a process in which the size of particle is changed to promote desired properties in a tablet.

Advantages of sizing include:

- Improved tablet-to-tablet content uniformity by virtue of increased number of particles per unit weight.
- Controlled particle size distribution of dry granulation or mix to promote better flow of mixture in tablet machine.
- Improved flow properties of raw materials.

- Improved color and/or active ingredient dispersion in tablet excipients.
- Uniformly sized wet granulation to promote uniform drying. There are also certain disadvantages associated with this unit operation if not controlled properly. They are as follows:
- A possible change in polymorphic form of the active ingredient, rendering it less or totally inactive, or unstable.
- A decrease in bulk density of active compound and/or excipients, which may cause flow problem and segregation in the mix.
- An increase in surface area from size reduction may promote the adsorption of air, which may inhibit wettability of the drug to the extent that it becomes the limiting factor in dissolution rate.

A number of different types of machines may be used for dry sizing or milling depending on whether gentle screening or particle milling is needed. The ranges of equipment employed for this process includes Fluid energy mill, Colloidal mill, Ball mill, Hammer mill, Cutting mill, Roller mill, Conical mill, etc.

3. Powder Blending

The successful mixing of powder is acknowledged to be more difficult unit operation because, unlike the situation with liquid, perfect homogeneity is practically unattainable. In practice, problems also arise because of the inherent cohesiveness and resistance to movement between the individual particles. The process is further complicated in many systems, by the presence of substantial segregation influencing the powder mix. They arise because of differences in size, shape, surface morphology, density of the component particles etc. The powder/granules blending is involved at pre granulation and/or post granulation stage of tablet manufacturing. Each process of mixing has optimum mixing time and so prolonged mixing may result in an undesired product. So, the optimum mixing time and mixing speed are to be evaluated. Blending step prior to compression is normally achieved in a simple tumble blender. The blender may be a fixed blender into which the powders are charged, blended and discharged.

4. 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:

(i) Wet granulation and (ii) Dry granulation

Ideal characteristics of granules

The ideal characteristics of granules include spherical shape, smaller particle size distribution with sufficient fines to fill void spaces between granules, adequate moisture (between 1-2%), good flow, good compressibility and sufficient hardness.

The effectiveness of granulation depends on the following properties:

- Particle size of the drug and excipients
- Type of binder (strong or weak)
- Volume of binder (less or more)
- Wet massing time (less or more)
- Amount of shear applied
- Drying rate (Hydrate formation and polymorphism)

(i) Wet granulation

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. However, these methods are affected by the equipment variables. Hence, additional process monitoring techniques would be valuable.

❖ Important steps involved in wet granulation

1. Mixing of drug(s) and excipients.
2. Preparation of binder solution.
3. Mixing of binder solution with powder mixture to form wet mass.
4. Course screening of wet mass using a suitable sieve (6-12 screens).
5. Drying of moist granules.
6. Screening of dry granules through a suitable sieve (14-20 screen).
7. Mixing of screened granules with disintegrant, glidant, and lubricant.

❖ Limitation of wet granulation

- The greatest disadvantage of wet granulation is its cost. It is an expensive process because of labor, time, equipment, energy and space requirements.
- Loss of material during various stages of processing.
- Stability may be a major concern for moisture sensitive or thermolabile drugs.
- An inherent limitation of wet granulation is that any incompatibility between formulation components is aggravated.

❖ Special wet granulation techniques:

- High shear mixture granulation
- Fluid bed granulation
- Extrusion-spheronization
- Spray drying

(ii) Dry granulation

In dry granulation process the powder mixture is compressed without the use of heat
and solvent. The two basic procedures are to form a compact of material by compression and then to mill the compact to obtain granules. Two methods are used for dry granulation. The more widely used method is slugging, where the powder is precompressed and the resulting tablets or slugs are milled to yield granules. The other method is to precompress the powder with pressure rolls using a machine such as Chilosonator.

❖ **Advantages:**

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
- For improved disintegration since powder particles are not bonded together by a binder

❖ **Disadvantages:**

- It requires a specialized heavy duty tablet press to form slug.
- It does not permit uniform color distribution as can be achieved with wet granulation where the dye can be incorporated into binder liquid.
- The process tends to create more dust than wet granulation, increasing the potential contamination.

Steps in dry granulation:

1. Milling of drugs and excipients
2. Mixing of milled powders
3. Compression into large, hard tablets to make slug
4. Screening of slugs
5. Mixing with lubricant and disintegrating agent
6. Tablet compression

Two main dry granulation processes:

a. Slugging process

Granulation by slugging is the process of compressing dry powder of tablet formulation with tablet press having die cavity large enough in diameter to fill quickly. The accuracy or condition of slug is not too important. Only sufficient pressure to compact the powder into uniform slugs should be used. Once slugs are produced they are reduced to appropriate granule size for final compression by screening and milling.

b. Roller compaction

The compaction of powder by means of pressure roll can also be accomplished by a machine called Chilosonator. Unlike tablet machine, the Chilosonator turns out a compacted mass in a steady continuous flow. The powder is fed down between the rollers from the hopper which contains a spiral auger to feed the powder into the compaction zone. Like slugs, the aggregates are screened or milled for production into granules.

(iii) Direct compression [3, 7]

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.

Advantages:

- Direct compression is more efficient and economical process as compared to other processes, because it involves only dry blending and compaction of API and necessary excipients.
- The most important advantage of direct compression is that it is an economical process. Reduced processing time, reduced labor costs, fewer manufacturing steps, and less number of equipments is required, less process validation, reduced consumption of power.
- Elimination of heat and moisture, thus increasing not only the stability but also the suitability of the process for thermolabile and moisture sensitive API.
- Particle size uniformity.
- Prime particle dissolution.
- In case of directly compressed tablets after disintegration, each primary drug particle is liberated. While in the case of tablets prepared 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.

Disadvantages:

Excipients Related

- Problems in the uniform distribution of low dose drugs.
- High dose drugs having high bulk volume, poor compressibility and poor flowability are not suitable for direct compression for example, Aluminum Hydroxide, Magnesium Hydroxide.
- The choice of excipients for direct compression is extremely critical. Direct compression diluents and binders must possess both good compressibility and good flowability.
- Many active ingredients are not compressible either in crystalline or amorphous forms.

Process Related

- Capping, lamination, splitting, or layering of tablets is sometimes related to air entrapment during direct compression. When air is trapped, the resulting tablets expand when the pressure of tablet is released, resulting in splits or layers in the tablet.
- In some cases require greater sophistication in blending and compression equipments.
- Direct compression equipments are expensive.

2 List of advancement technique in Granulations

- Steam Granulation
- Melt Granulation / Thermoplastic Granulation
- Moisture Activated Dry Granulation (MADG)
- Moist Granulation Technique (MGT)
- Thermal Adhesion Granulation Process (TAGP)
- Foam Granulation

5. Drying

Drying is a mass transfer process resulting in the removal of water from a solid by evaporation. The essential constituents of an effective piece of drying equipment are heat supply to increase the temperature and thereby reduce relative humidity, a device for removal of evaporated water and a means of minimizing the distance that water molecules must diffuse before they can be evaporated.

The fluidized bed drier is the most commonly used device for drying tablet granules. The solid is fluidized from below by a jet of hot air, and so each granule is separated from its neighboring granules. The air provides an effective means of heat transfer, as well as of removing water vapors. The speed of the drying process is governed by the distance that water molecules must diffuse before

they arrive at the evaporative surface. Since the wet granules are present as individual units, the maximum distance over which diffusion occurs is equal to the radius of a granule. Hence, fluidized bed drying is a rapid process.A more traditional means of drying is the tray drier. Hot air flows over a series of shelves on which the wet material is spread. Compared to the fluidized bed drier, the solid-air interface is smaller, and water molecules may have to diffuse through the whole thickness of the solid layer before the evaporative surface is reached. Thus, the drying process is slower in a tray drier than in a fluidized bed drier.

6. Compression

During compression (Figure 1.1), the bulk volume of the material is reduced, resulting in the displacement of the gaseous phase (air). Further increasing the force leads to particle deformation and rearrangement. At this point, the three principal modes of deformation are as follows:

A. Elastic deformation: A spontaneously reversible deformation of the compact in which, upon removal of the load, the powder mass reverts back to its original form. Most materials undergo elastic deformation to some extent. Compression of rubber would be by elastic deformation.

B. Plastic deformation: After exceeding the elastic limit of the material (yield point), the deformation may become plastic, that is, the particles undergo viscous flow. This is the predominant mechanism when the shear strength between the particles is less than the tensile or breaking strength. Plastic deformation is a time-dependent process.

C. Brittle fracture: Upon exceeding the elastic limit of the material (yield point), the particles undergo brittle fracture if the shear strength between the particles is greater than the tensile or breaking strength. Under these conditions, the larger particles are sheared and broken into smaller particles. Since some of these deformation characteristics are time-dependent, machine characteristics can have a major effect on tableting performance. These characteristics determine the rate of force application, dwell time (i.e., the time of maximum compression force, which depends on the punch head flat diameter and the tangential velocity), and the rate of decompression.

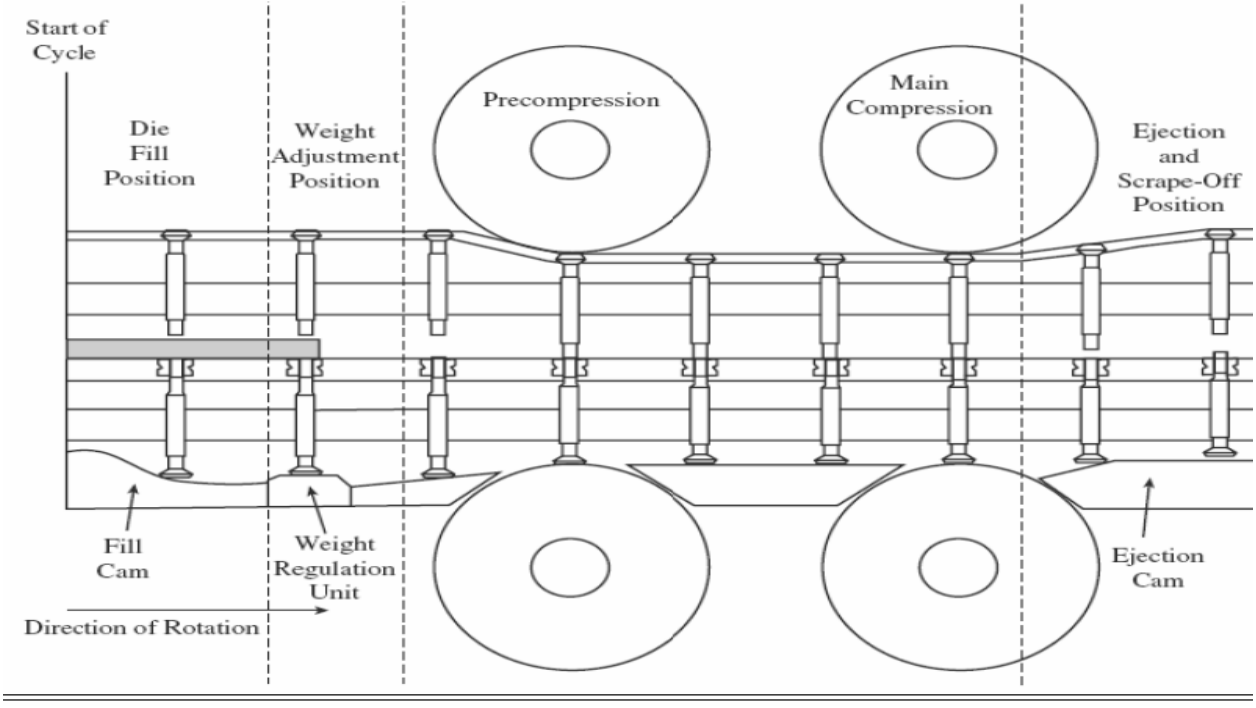

Figure 1: Compression Process

Problems in Tablet Manufacturing

An ideal tablet should be free from any visual defect or functional defect. The advancements and innovations in tablet manufacture have not decreased the problems, often encountered in the production, instead have increased the problems, mainly because of the complexities of tablet presses; and/or the greater demands of quality. An industrial pharmacist usually encounters number of problems during manufacturing. Majority of visual defects are due to inadequate fines or inadequate moisture in the granules ready for compression or due to faulty machine setting.

Functional defects are due to faulty formulation. Solving many of the manufacturing problems requires an in-depth knowledge of granulation processing and tablet presses, and is acquired only through an exhaustive study and a rich experience.

Following are the defects that are found during tablet manufacturing

- Capping
- Lamination / Laminating
- Chipping
- Cracking
- Sticking / Filming
- Picking
- Binding
- Mottling
- Double impression
-

 ISSN: 2250-1177 CODEN (USA): JDDTAO

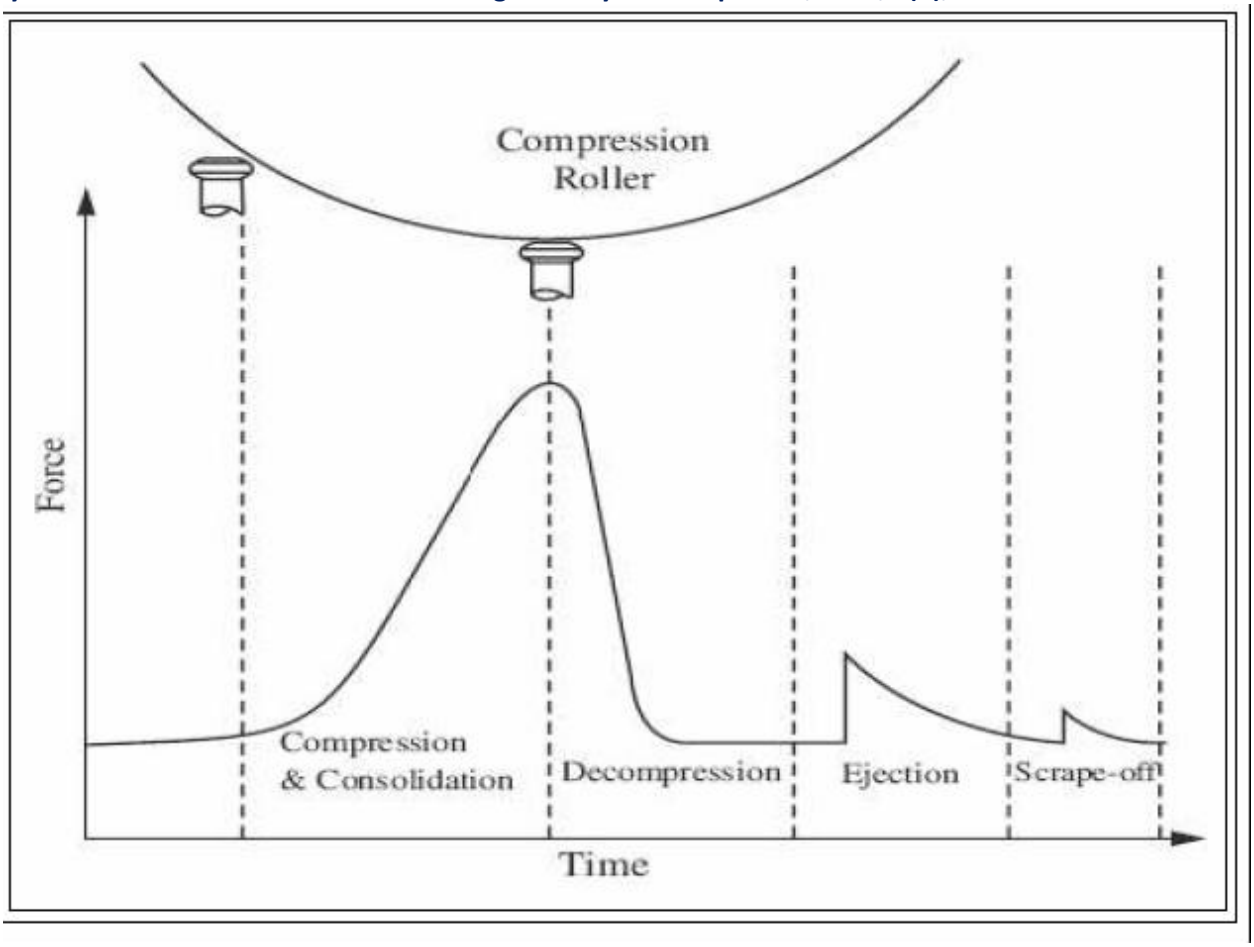

Figure 2: Forces and Time Relationship

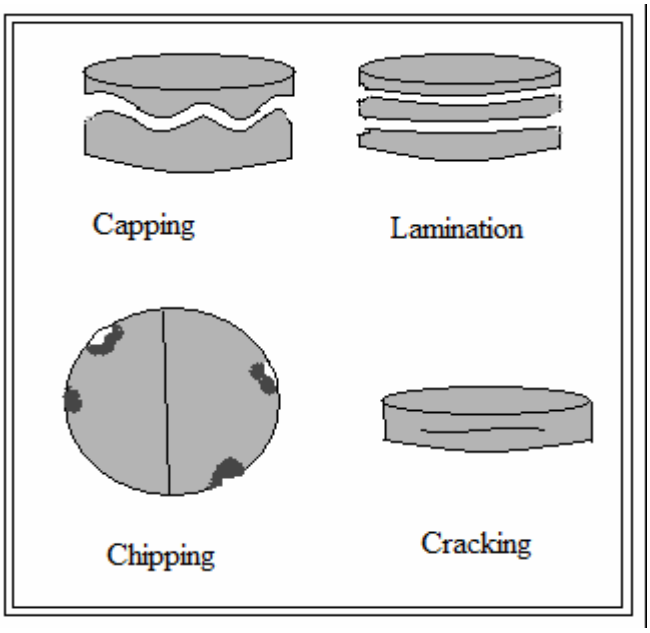

Figure 3: Tablet Defects

Evaluation parameter

To design tablet and later monitor tablet production quality, quantitative evaluation and assessment of tablets chemical, physical and bioavailability properties needs to be evaluated by using following parameters.

- General appearance
- Unique identification marking
- Organoleptic properties
- Hardness and friability
- Weight variation
- Drug content
- Disintegration time
- Dissolution profile
- Impurity profile

Ideal characteristics of excipients

 ISSN: 2250-1177 CODEN (USA): JDDTAO

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

Introduction to Immediate Release Dosage Form :

Pharmaceutical products designed for oral delivery and currently available on the prescription and over-the-counter markets are mostly the immediate release type, which are designed for immediate release of drug for rapid absorption. Disintegrating agents are substances routinely included in tablet formulations and in some hard shell capsule formulations to promote moisture penetration and dispersion of the matrix of the dosage form in dissolution fluids. Superdisintegrant improve disintegrant efficiency resulting in decreased use levels when compared to traditional disintegrants. Traditionally, starch has been the disintegrant of choice in tablet formulation, and it is still widely used. For instance, starch generally has to be present at levels greater than 5% to adversely affect compatibility, especially in direct compression. Drug release from a solid dosage form can be enhanced by addition of suitable disintegrants.

- Mechanism of Disintegrants*:*

1) High swellability

2) Capillary action and high swellability

3) Chemical reaction

When introduced to an aqueous environment of use, the tablet rapidly takes up water, leading to swelling of the disintegrant and rapid disintegration of the tablet before the dispersion polymer can form a hydrogel. The disintegrant should be chosen such that it (1) swells rapidly when introduced into the use environment and (2) has a low tendency to form or promote formation of a hydrogel. The rate of swelling of the disintegrant is directly correlated to tablet disintegration times. Tablets containing disintegrants cause more rapid swelling have faster disintegration times at comparable disintegrant levels.

The amount of work, W, or swelling energy, due to swelling can be measured using a dynamic mechanical analyzer (DMA). The swelling energy attributable to swelling of the disintegrant in the compact may be calculated from the following equation:

$$W = P\Delta V$$

Where W is the work or swelling energy of the disintegrant, P is the pressure applied by the probe, and ΔV is the volume change of the sample.

To compare disintegrants, the swelling energy per mass of disintegrant is used. Preferably, the disintegrant generates a swelling energy of at least 0.05 J/g within about 10 minutes following addition of water to the liquid reservoir.

The most popular disintegrants are corn starch, soluble starch etc. which have been well dried and powdered. Starches have great affinity for water and swell when moistened thus facilitating the rupture of the tablet matrix, its disintegration action in tablets is due to capillary action. Spherical shape of starch increases the porosity of tablet thus promoting capillary action.

Classification of "Superdisintegrant" may be organized into three classes based on their chemical structure. As shown in Table below.

Table 1: List of Disintegrants

Disintegrants	Concentration in granules (%w/w)	Special comments
Starch USP	5-20	Higher amount is required, poorly compressible
Starch 1500	5-15	-
Avicel®(PH 101, PH 102)	10-20	Lubricant properties and directly compressible
Solka floc®	5-15	Purified wood cellulose
Alginic acid	1-5	Acts by swelling
Na alginate	2.5-10	Acts by swelling
Explotab®	2-8	Sodium starch glycolate, superdisintegrant.
Polyplasdone®(XL)	0.5-5	Cross-linked PVP
Amberlite® (IPR 88)	0.5-5	Ion exchange resin
Methyl cellulose, Na CMC, HPMC	5-10	-
AC-Di-Sol®	1-3	Direct compression
	2-4	Wet granulation

❖ **Incorporation into Immediate Release Dosage Forms**

The immediate release dosage form comprises the dispersion, a porosigen, and a disintegrant. The dosage form is in the form of a compressed tablet or other solid dosage form. Other conventional formulation excipients may be employed in the dosage forms including surfactants, pH modifiers, fillers, matrix materials,

 ISSN: 2250-1177 CODEN (USA): JDDTAO

complexing agents, solubilizers, pigments, lubricants, glidants, flavorants, may be used for customary purposes and in typical amounts without adversely affecting the properties of the compositions.

➢ **Solid Dispersion:**

The dosage forms contain a high loading of the solid amorphous dispersion. High loadings of dispersion in the dosage form minimize the size of the dosage form, making it easier for the patient to swallow it and improving patient compliance. Depending on the drug dose, the immediate release dosage form comprises at least 30-50 wt % of the dispersion.

This type of dosage forms disintegrates within 10 minutes following introduction to a disintegration medium. The dosage form of the present invention releases at least 70 wt %, more preferably at least 80 wt % and most preferably at least 90 wt % of the low solubility drug within 35 minutes following introduction to a dissolution medium.

➢ **Concentration-Enhancing Polymers:**

Concentration enhancing polymers suitable for use in the solid drug dispersions in the sense that they do not chemically react with the drug in an adverse manner. The polymer can be neutral or ionizable, and should have an aqueous solubility of at least 0.1 mg/mL over at least a portion of the pH range of 1-8.

It is preferred that the concentration-enhancing polymer be "amphiphilic" in nature, meaning that the polymer has hydrophobic and hydrophilic portions. It is believed that such polymers have relatively strong interactions with the drug and may promote the formation of various types of polymer/drug assemblies in solution.

A particularly preferred class of amphiphilic polymers is those that are ionizable noncellulosic polymers. Exemplary polymers include: carboxylic acid-functionalized vinyl polymers, such as the carboxylic acid-functionalized polymethacrylates and polyacrylates such as the Eudragit; amine-functionalized polyacrylates and polymethacrylates; proteins, such as gelatin and albumin; and carboxylic acidfunctionalized starches such as starch glycolate. Another class of polymers suitable for use comprises non-ionizable or neutral non-cellulosic polymers. Exemplary polymers include: vinyl polymers and copolymers having at least one substituent selected from the group consisting of hydroxyl, alkylacyloxy, and cyclicamido; polyvinyl alcohols; polyvinyl alcohol polyvinyl acetate copolymers; polyvinyl pyrrolidone; polyethylene polyvinyl alcohol copolymers.

The amount of concentration-enhancing polymer relative to the amount of drug present in the solid drug dispersions depends on the drug and concentration-enhancing polymer and may vary widely from a drug-to-polymer weight ratio of 0.01 to 5, or from about 1 to about 80 wt % drugs. However, in most cases, except when the drug dose is quite low, i.e., 25 mg or less, it is preferred that the drug-to-polymer ratio is greater than 0.05 and less than 2.5. The maximum drug: polymer ratio that yields satisfactory results varies from drug to drug and is best determined in the in vitro and/or in vivo dissolution tests.

➢ **Preparation of Dispersions:**

Different methods are also been used for preparation of solid dispersions such as Melting method, Solvent method, Melting solvent method (melt evaporation), Melt extrusion method, Lyophilisation Technique, Melt Agglomeration Process, The Use Of Surfactant, Electrospinning and Super Critical Fluid Technology.

➢ **Disintegrants:**

As disintegrants sodium starch glycolate(SSG), sodium carboxymethyl cellulose, calcium carboxymethyl cellulose, croscarmellose sodium, Crospovidone, polyvinyl polypyrrolidone, methyl cellulose, microcrystalline cellulose, powdered cellulose, lower alkyl-substituted hydroxypropyl cellulose, polacrilin potassium, starch, pregelatinized starch, sodium alginate, and mixtures thereof. The amount of disintegrant included in the dosage form will depend on several factors, including the properties of the dispersion, the properties of the porosigen and the properties of the disintegrant selected. Generally, the disintegrant will comprise from 1 wt % to 25 wt % of the dosage form.

➢ **Porosigen:**

The dosage form also includes a porosigen. A "porosigen" is a material that, when present in the formulation containing the solid amorphous dispersion, leads to a high porosity and high strength following compression of the blend into a tablet. In addition, preferred porosigen are soluble in an acidic environment with aqueous solubility typically greater than 1 mg/mL at a pH less than about 5. Examples of porosigens include acacia, calcium carbonate, calcium sulfate, calcium sulfate dihydrate, compressible sugar, dibasic calcium phosphate, tribasic calcium phosphate, monobasic sodium phosphate, dibasic sodium phosphate, lactose, magnesium oxide, magnesium carbonate, silicon dioxide, magnesium aluminum silicate, maltodextrin, mannitol, methyl cellulose, microcrystalline cellulose, sorbitol, sucrose, xylitol and mixtures thereof. Generally, the porosigen will comprise from 5 to 70 wt %. To ensure the tablet has sufficient porosity to allow adequate wicking of water into the tablet to cause rapid tablet disintegration and/or rapid release of drug, tablet porosity should be within 0.15-0.25. Accordingly, the disintegrant and porosigen should be selected so that the immediate release dosage form has high strength as well as the high porosity required to achieve rapid disintegration and/or release of drug.

➢ **Surfactants:**

One very useful class of excipients is surfactants, preferably present from 0 to 10 wt %. Suitable surfactants include fatty acid and alkyl sulfonates; commercial surfactants such as benzalkonium chloride, dioctyl sodium sulfosuccinate, polyoxyethylene sorbitan fatty acid esters, natural surfactants such as sodium taurocholic acid, lecithin, and other phospholipids and mono- and diglycerides; and mixtures thereof. Such materials can advantageously be employed to increase the rate of dissolution by, for example, facilitating wetting, or otherwise increase the rate of drug release from the dosage form.

➢ **pH Modifiers:**

Inclusion of pH modifiers such as acids, bases, or buffers may also be beneficial in an amount of from 0 to 10 wt %. Acidic pH modifiers (e.g., acids such as citric acid or succinic acid) retard the dissolution of the pharmaceutical composition when the dispersion polymer is anionic. Alternatively, basic pH modifiers (e.g., sodium acetate or

 ISSN: 2250-1177 CODEN (USA): JDDTAO

amines) enhance the rate of dissolution of the same types of pharmaceutical composition.

- **Diluents:**

Examples of other matrix materials, fillers, or diluents include lactose, mannitol, xylitol, dextrose, sucrose, sorbitol, compressible sugar, microcrystalline cellulose, powdered cellulose, starch, pregelatinized starch, dextrates, dextran, dextrin, dextrose, maltodextrin, calcium carbonate, dibasic calcium phosphate, tribasic calcium phosphate, calcium sulfate, magnesium carbonate, magnesium oxide, poloxamers, polyethylene oxide, hydroxypropyl methyl cellulose and mixtures thereof.

- **Surface Active Agents:**

Sodium lauryl sulfate and polysorbate 80. Drug-complexing agents or solubilizers include the polyethylene glycols, caffeine, xanthene, gentisic acid and cylodextrins.

- **Lubricants:**

Examples of lubricants include calcium stearate, glyceryl monostearate, glyceryl palmitostearate, hydrogenated vegetable oil, light mineral oil, magnesium stearate, mineral oil, polyethylene glycol, sodium benzoate, sodium lauryl sulfate, sodium stearyl fumarate, stearic acid, talc and zinc stearate.

- **Glidants:**

Examples of glidants include silicon dioxide, talc and cornstarch. Preferably from 10 to 50 wt % of the dosage form Tablets are generally formed by blending the dispersion, disintegrant, and porosigen with optional excipients and then compressing the powder to form tablets. Often it is desirable to granulate the compositions, with or without the addition of excipients prior to compression. For example, the dispersion, disintegrant, and porosigen may be granulated by mechanical means for example, roller compaction or "slugging," followed by milling to form granules. The granules typically have improved flow, handling, blending, and compression properties relative to the ungranulated materials. Wet granulation techniques may also be employed, provided the solvents and process selected do not alter the properties of the solid amorphous dispersion. Improved wetting, disintegrating, dispersing and dissolution properties may be obtained by the inclusion of other excipients.

After the tablet is formed by compression, it is desired that the tablet has "strength" of at least 5-10 Kp/cm2. Here, "strength" is the fracture force, also known as the tablet "hardness," required to fracture a tablet formed from the materials. The fracture force may be measured using a Schleuniger Tablet Hardness Tester. Friability is a wellknown measure of a tablet's resistance to surface abrasion that measures weight loss in percentage after subjecting the tablets to a standardized agitation procedure. Friability values of from 0.8 to 1.0% are regarded as constituting the upper limit of acceptability.

DRUG AND EXCIPIENT

S. NO.	MATERIALS	GRADE	MANUFACTURER
1.	Olmesartan medoxomile	A.R	Purchased from Seva fine chem, Ahmedabad.
2.	Micro crytalline cellulose	L.R.	Amneal pharmaceutical pvt Ltd., Ahmedabad.
3.	Pregelatinized Starch	L.R.	Amneal pharmaceutical pvt Ltd., Ahmedabad.
4.	Sodium Starch Glycolate	L.R.	Amneal pharmaceutical pvt Ltd., Ahmedabad
5.	Lactose monohydrate	L.R.	S d fine-chem limited. Mumbai.
6.	Hydroxy propyl cellulose	L.R.	Amneal pharmaceutical pvt Ltd., Ahmedabad.
7.	Magnesium Staerate	L.R.	Amneal pharmaceutical pvt Ltd., Ahmedabad.
8.	Sodium stearyl fumarate	L.R.	Merck specialities private limited, Mumbai.
9.	Talc	L.R	Central drug house (P) Ltd., New Delhi.

EQUIPMENTS USED:

S. No.	INSTRUMENTS	MANUFACTURER
1.	Electronic Weighing Balance	Essae-Teraoka Ltd, Model No. IND/09/2001/28
2.	UV-Vis Spectrophotometer (UV-1800)	Shimadzu, Japan.
3.	FTIR Spectrophotometer	Shimadzu, Japan.
4.	Electronic Weighing Balance	Remi Equipments, Mumbai.
5.	Dissolution test apparatus TDT-08T	ElectroLab, Mumbai.
6.	Digital vernier caliper	Mitutoyo, Japan.
7.	Digital pH meter 7007	Digisun Electronics Hyderabad.
8.	Test Sieve (No.16, 22, 40, 60, 80)	Scientific Engineering Corp. Delhi.
9.	Hot Air Oven	Servewell Instrument PVT LTD, Bangalore.
10.	Stability Chamber	Lab Control Equipment Co. Mumbai.
11.	Friabilator USP EF-2	ElectroLab, Mumbai.
12.	Monsanto Hardness Tester	Ketan engineering Ltd, Mumbai
13.	Tablet punching machine, Rimek mini press-1	Karnavati Engineering Ltd, Mehsana, Gujarat.
14.	Melting Point Apparatus	SETCO Ltd, Bangalore.

Physico-mechanical characterization

Bulk Density:

It refers to packing of particles. Bulk density is used to determine the amount of drug that occupies the volume in g/ml.

Procedure: Weighed quantity (10gm) of Drug X was transferred into 100 ml measuring cylinder without tapping during transfer. The volume occupied by drug was measured. Bulk density was measured by using formula

$$\rho_i = m / V_i$$

Where, m = mass of the blend

V_i = untapped volume

Tapped density:

Weighed quantity (10gm) of drug was taken into a graduated cylinder. Volume occupied by the drug was noted down. Then the cylinder was subjected to 500, 750 &1250 taps in tap density apparatus (Electro Lab USP II). According to USP, The blend was subjected for 500 taps. % Volume variation was calculated and subjected for additional 750 taps. % Variation is calculated.

$$\rho_t = m/V_t$$

Where, V_t is tapped volume

Carr's Index (Compressibility):

The compressibility index and Hausner ratio are measures of the property of powder to be compressed. The packing ability of drug was evaluated from change in volume, which is due to rearrangement of packing occurring during tapping. It was indicated as Carr's compressibility index was calculated as follows.

Carr's index = [Tapped density - Bulk density/Tapped density] X 100

Hausner Ratio: It is measurement of frictional resistance of the drug .The ideal range should be 1.2-1.5. It was determined by the ratio of tapped density and bulk density

Hausner Ratio = Tapped density / Bulk density

Angle of Repose:

It is defined as the maximum angle that can be obtained between the free standing of powder heap and horizontal plane, which is given by the equation:

$$\theta = \tan^{-1} h/r$$

Where, θ = Angle of repose.

h = Height of powder heap.

r = Radius of the powder cone.

REFERENCE:

1. Aulton ME. "Pharmaceutics" The Science of dosage form design; 2nd Ed. Churchill livingstone. 2002: 398, 365-374, 414-418.
2. Lachman L, Lieberman HA, Kanig JL. The Theory and Practice of Industrial Pharmacy. Tablets; 3rd Ed. Varghese publishing house, Bombay. 1987:294, 336, 413.
3. Lieberman HA, Lachman L, Schwartz JB. Pharmaceutical Dosage Forms: Tablets, Marcel Dekker Inc, New York. Vol 1,2nd Ed: 195-229.
4. Basic consideration of tablets. Available from [cited on 2011 Mar 17] URL: http://en.wikipedia.org/wiki/Tablet
5. Melkebeke BV, Vervaet C, Remon JP. Validation of a continuous granulation process using a twin-screw extruder. Inter. J of Pharm. 2008; 356:224-230.
6. Swarbrick J. Encyclopedia of Pharmaceutical Technology. Informa Healthcare USA, Inc., New York. 3rd Ed: 3641, 3657-59, 3612-13, 3928.
7. Granulation Techniques, Drying process in tablet manufacturing. [cited on 2011 Mar 22] Available from URL: http://www.pharmapedia.com.
8. Allen LV, Popovich NG, Ansel HC. Ansel's Pharmaceutical Dosage Forms and Drug Delivery Systems. Lippincott Williams and Wilkins, Baltimore USA. 8th Ed. 2006:239-244.
9. Jorgensen AC. Increasing process understanding of wet granulation by spectroscopic methods and dimension reduction tools. Faculty of Pharmacy of the University of Helsinki. Oct 2004.
10. Parikh DM. Theory of Granulation, Handbook of Pharmaceutical Granulation Technology. 2nd Ed. 2005:7-33.
11. Chien YW. Novel drug delivery systems. Marcel Dekker Inc. 2nd Ed. 1992:139-40.
12. Leah E, Appel DT, Friesen JE, Byers MD, Crew BC, Hancock SJ, Schadtle. Immediate release dosage forms containing solid drug dispersion. United States Patent No. 424465; 2002.
13. US-FDA guideline. Page no: 46-73.
14. Castell D., Ralph E. Small, Review of immediate-release omeprazole for the treatment of gastric acid-related disorders,2005 vol.-2,Page no:698-713.

