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A REVIEW ON MOUTH DISSOLVING TABLETS

Tarun Kumar Guleri*, Loveleen Preet Kaur, Tanu Kumar, Nishu Dixit

Dept of Pharmaceutics, Sri Sai College of Pharmacy, Pathankot, Punjab State, India.

ABSTRACT

Oral route has been one of the most popular routes of drug delivery due to its ease of administration, patient compliance, least sterility constraints and flexible design of dosage forms. Recently, Mouth-dissolving drug delivery systems have started gaining popularity and acceptance as new drug delivery systems, because they are easy to administer and lead to better patient compliance. Usually, elderly people experience difficulty in swallowing the conventional dosage forms (tablets, capsules, solutions and suspensions) because of tremors of extremities and dysphasia. Mouth -dissolving drug delivery systems may offer a solution for these problems.

Keywords: Mouth Dissolving Tablet, Oral drug delivery system, Method of preparation, Evaluation.

INTRODUCTION

For many decades treatment of an acute disease or chronic illness has mostly accomplished by delivery of drugs to patients using conventional drug delivery system. Even today these conventional drug delivery systems are the primary pharmaceutical products commonly seen in the prescription. Conventional oral drug products are formulated to release the active principle immediately after oral administration to obtain rapid and complete systemic drug absorption.

Drug absorption is defined as the process of movement of unchanged drug from the site of administration to systemic circulation. Systemic drug absorption from a drug product consists of a succession of rate process for solid oral, immediate release drug products [1].

The rate process include

- Dissolution of the drug in an aqueous environment.
- Absorption across cell membranes into systemic circulation.

For drugs that have very poor aqueous solubility, the rate at which the drug dissolves (dissolution) is often the slowest step and therefore exhibits a rate limiting effect on drug bioavailability. In contrast, for a drug that has a high aqueous solubility the dissolution rate is rapid the rate at slowest or rate limiting step [2,3]. Together with the permeability, the solubility behavior of a drug is a key which the drug crosses or permeates cell membrane is the determinant of its oral bioavailability. They have always been certain drugs for which solubility has presented a challenge to the development of a suitable formulation for oral administration. Examples such as griseofulvin, digoxin, phenytoin, sulphathiazole& chloramphenicol come immediately to mind. Recent advances in Novel Drug Delivery System (NDDS) aims to enhance safety and efficacy of already used drug molecule by formulating a convenient dosage forms for administration and to achieve better patient compliance. To develop a chemical entity, a lot of money, hard work and time are required. So, focus is rather being laid on the development of new drug delivery systems for already existing drugs, with enhanced efficacy and bioavailability, thus reducing the dose and dosing frequency to minimize the side effects [2].

The oral route of administration is the most preferred route due to its many advantages like ease of administration, accurate dosage, self-medication, pain avoidance, versatility and patient compliance. The most popular dosage forms being tablets and capsules, one important drawback of these dosage forms however is the difficulty to swallow.

Corresponding Author: - **Tarun Kumar Guleri** Email: tarunsharmaguleri@gmail.com

It is estimated that 50% of the population is affected by this problem which results in a high incidence of non-compliance and ineffective therapy. The difficulty is experienced in particular by pediatric and geriatric patients, but it also applies to people who are ill in bed and to those active working patients who are busy or traveling, especially those who have no access to water and also in following conditions like: Parkinsonism, Motion sickness, Unconsciousness and Mentally disabled persons. To fulfill these medical needs, the pharmaceutical technologists have developed a novel type of dosage form for oral administration, the Mouth Dissolving Tablets (MDT), tablets that disintegrate and dissolve rapidly in saliva without water.

MOUTH DISSOLVING TABLETS

The mouth dissolving tablets usually dissolve in the oral cavity within 15 seconds to 3 minutes. In another words a Mouth-dissolving tablet is tablet that dissolves or disintegrates in the oral cavity without the need of water or chewing. Mouth dissolving tablets are also called as Orodispersible tablets, Quick disintegrating tablets, Mouth dissolving tablets, Oral rapid disintegrating tablets, Rapid dissolving tablets, Porous tablets and Rapimelts. However, of all the above terms, United States Pharmacopoeia (USP) approved those dosage forms as Orally Disintegrating Tablets (ORALLY DISINTEGRATING TABLETS). Recently European Pharmacopoeia has used the term Orodispersible tablet for tablets that disperses readily and within three minutes in mouth before swallowing.

United States Food and Drug Administration (USFDA) define Orally Disintegrating Tablets as "A solid dosage form containing medicinal substances or an active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon tongue". The disintegration time for mouth dissolving tablets generally ranges from several seconds to about a minute.

ADVANTAGES OF MOUTH DISSOLVING DRUG DELIVERY SYSTEM

- Ease of administration to pediatric, geriatric patients and psychiatric patients.
- Free of the risk of suffocation due to physical obstruction when swallowed, thus offering improved safety.
- Convenience of administration accurate dose as compared to liquids.
- Having good mouths feel property.
- No need of water to swallow the dosage from.
- Rapid dissolution of drug and absorption, which may produce rapid onset of action from the mouth, pharynx and esophagus.
- Pre gastric absorption can result in improved bioavailability, reduced dose and improved clinical performance by reducing side effects.
- New business opportunities: product differentiation, line extension and life-cycle management, exclusivity of product promotion and patent-life extension [3].

LIMITATIONS OF MOUTH DISSOLVING TABLETS

- Drugs with relatively larger doses are difficult to formulate into MDT e.g. antibiotics like ciprofloxacin with adult dose tablet containing about 500 mg of the drug.
- Patients who concurrently take anticholinergic medications may not be the best candidates for MDT. Similarly patients with Sjögren's syndrome or dryness of the mouth due to decreased saliva production may not be good candidates for these tablet formulations.
- The tablets usually have insufficient mechanical strength. Hence, careful handling is required.
- The tablets may leave unpleasant taste and/or grittiness in mouth if not formulated properly [4].

CHALLENGES TO DEVELOP MOUTH DISSOLVING TABLET

I) Mechanical strength and disintegration time-

Orally Disintegrating Tablets are formulated to obtain disintegration time usually less than a minute. While doing so, maintaining a good mechanical strength is a prime challenge. Many ORALLY DISINTEGRATING TABLETSs are fragile and there are many chances that such fragile tablet will break during packing, transport or handling by the patients. Tablets based on technologies like Zydis need special type of packaging. It is very natural that increasing the mechanical strength will delay the disintegration time. So, a good compromise between these two parameters is always essential.

II) Taste masking

Many drugs are bitter in taste. A tablet of bitter drug dissolving/ disintegration in mouth will seriously affect patient compliance and acceptance for the dosage form. So, effective taste masking of the bitter drugs must be done so that the taste of the drug is not felt in the oral cavity.

III) Mouth feel

The Orally Disintegrating Tablets should not disintegrate into larger particles in the oral cavity. The particles generated after disintegration of the Orally Disintegrating Tablets should be as small as possible. Orally Disintegrating Tablets should leave minimal or no residue in mouth after oral administration. Moreover addition of flavours and cooling agents like menthol improve the mouth feel.

IV) Sensitivity to environmental conditions

Orally Disintegrating Tablets generally should exhibit low sensitivity to environment conditions such as

humidity and temperature as most of the materials used in an Orally Disintegrating Tablets are meant to dissolve in minimum quantity of water.

V) Amount of drug

For lyophilized dosage forms, the drug dose must be lower than 400 mg for insoluble drugs and less than 60 mg for soluble drugs.

VI) Aqueous solubility

Water-soluble drugs form eutectic mixtures, which result in freezing-point depression and the formation of a glassy solid that may collapse upon drying because of loss of supporting structure during the sublimation process.

VII) Size of tablet

It has been reported that the easiest size of tablet to swallow is 7-8 mm while the easiest size to handle was larger than 8 mm. Therefore, the tablet size that is both easy to take and easy to handle is difficult to achieve.

VIII) Cost

The technology used for an Orally Disintegrating Tablets should be acceptable in terms of cost of the final product. Methods like Zydis and Orasolv that require special technologies and specific packaging increase the cost to a remarkable extent [5].

EXCIPIENTS USED IN MOUTH DISSOLVING TABLET

Super disintegrants

Crosspovidone, Microcrystalline cellulose, sodium starch glycollate, sodium carboxy methyl cellulose, pregelatinzed starch, calcium carboxy methyl cellulose, and modified corn starch. Sodium starch glycollate has good flowability than crosscarmellose sodium. Cross povidone is fibrous nature and highly compactable.

Flavours

Peppermint flavor, cooling flavor, flavor oils and flavoring aromatic oil, peppermint oil, clove oil, bay oil, anise oil, Cardamom flavor, eucalyptus oil thyme oil, oil of bitter almonds. Flavoring agents include, vanilla, citus oils, fruit essences

Sweeteners

Aspartame, Sugars derivatives

Fillers

Directly compressible spray dried Mannitol, Lactose, Dextrose, Sorbitol, xylitol, calcium carbonate, magnesium carbonate, calcium phosphate, calcium sulfate, pregelatinized starch, magnesium trisilicate, aluminium hydroxide.

Surface active agents

Sodium doecylsulfate, sodium lauryl sulfate, polyoxyethylene sorbitan fatty acid esters (Tweens), sorbitan fatty acid esters (Spans), polyoxyethylene stearates.

Lubricants

Stearic acid, Magnesium stearate, Zinc stearate, calcium stearate, talc, polyethylene glycol, liquid paraffin, magnesium lauryl sulfate, colloidal silicon dioxide [6].

SUPERDISINTEGRANTS

Disintegrants are substances routinely included in tablet formulations and in some hard shell capsule formulations to promote moisture penetration and dispersion of the matrix of dosage form in dissolution fluids. An oral solid dosage form should ideally disperse into the primary particles from which it was prepared. Superdisintegrants are generally used at a low concentration, typically 1-10% by weight relative to total weight of dosage unit. Generally employed superdisintegrants are croscarmellose sodium (Ac-Di-Sol), crospovidone (CP), sodium starch glycolate (SSG) etc. which represent example of cross-linked cellulose, cross-linked polymer and cross-linked starch respectively.

MECHANISM OF ACTION OF DISINTEGRANT

Various mechanisms proposed in this concern include water wicking, swelling, deformation recovery, repulsion and heat of wetting. It seems likely that no single mechanism can explain the complex behavior of the disintegrants. However, each of these proposed mechanisms provides some understanding of different aspects of disintegrant action.

I. Water wicking

The ability of disintegrant to draw water into the porous network of tablet is essential for effective disintegration. On keeping the tablet into suitable aqueous medium, the medium enters into tablet and replaces the air adsorbed on the particles which weakens the intermolecular bonds and breaks the tablet into fine particles. Water uptake by tablet depends upon hydrophilicity of the drug/excipients and on tableting conditions. Unlike swelling, which is mainly a measure of volume expansion with accompanying force generation, water wicking is not necessarily accompanied by a volume increase. The ability of a system to draw water can be summarized by

Washburn's equation:

$$L2 = (\gamma \cos\theta / 2\eta) \times rt$$

The Washburn equation is too simplistic to apply to a dynamic tablet disintegration process, but it does show that any change in the surface tension (γ), pore size (r), solid-liquid contact angle (θ) or liquid viscosity (η) could change the water wicking efficiency. L is the length

of water penetration in the capillary and t is the time. This process is also considered as capillary action method.

II. Swelling

Although water penetration is a necessary first step for disintegration, swelling is probably the most widely accepted mechanism of action for tablet disintegrants. For swelling to be effective as a mechanism of disintegration, there must be a superstructure against which disintegrant swells. Figur represents the disintegration of tablet by wicking and swelling. Swelling of the disintegrant against the matrix leads to development of a swelling force. A large internal porosity in the dosage form in which much of the swelling can be accommodated reduces the effectiveness of the disintegrant. On the other hand, sufficient swelling force is exerted in the tablet with low porosity. It is worthwhile to note that if packing fraction is very high, fluid is unable to penetrate in the tablet and disintegration is again slowed down.

III. Heat of wetting

When disintegrants with exothermic properties get wetted, localized stress is created due to capillary air expansion, which aids in disintegration of tablet. This explanation, however, is limited to only a few types of disintegrants and cannot describe the action of most modern disintegrating agents.

IV. Due to release of gases

Carbon dioxide gets released within tablets on wetting due to interaction between bicarbonate and carbonate with citric acid or tartaric acid. The tablet disintegrates due to generation of pressure within the tablet. This effervescent mixture is used when pharmacist needs to formulate very rapidly dissolving tablets or fast disintegrating tablet. As these disintegrants are highly sensitive to small changes in humidity level and temperature, strict control of environment is required during preparation of the tablets. The effervescent blend is either added immediately prior to compression or can be added into two separate fractions of formulation.

V. Particle repulsive forces

This is another mechanism of disintegration that attempts to explain the swelling of tablet made with non-swellable disintegrants. Guyot-Hermann proposed a particle-particle repulsion theory to explain the observation that particles which do not swell extensively such as starch, could still disintegrates tablets. According to this theory, water penetrates into tablet through hydrophilic pores and a continuous starch network is created that can convey water from one particle to the next, imparting a significant hydrostatic pressure. The water then penetrates between starch grains because of its affinity for starch surfaces, thereby breaking hydrogen bonds and other forces holding the tablet together. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it.

VI. Deformation recovery

Deformation recovery theory implies that the shape of disintegrant particles is distorted during compression and the particles return to their precompression shape upon wetting, thereby causing the tablet to break apart. Such a phenomenon may be an important aspect of the mechanism of action of disintegrants such as crospovidone and starch that exhibit little or no swelling. Disintegration of tablet by deformation as well as repulsion is illustrated in Figure.

VII. By enzymatic reaction

Enzymes present in the body also act as disintegrants. Due to swelling, pressure is exerted in the outer direction that causes the tablet to burst or the accelerated absorption of water leads to an enormous increase in the volume of granules to promote disintegration [7].

TECHNOLOGIES USED TO MANUFACTURE MOUTH DISSOLVING TABLET

CONVENTIONAL TECHNIQUES

Lyophilization or Freeze Drying

Formation of porous product in freeze-drying process is exploited in formulating Mouth dissolving tablets (MDT). Lyophilization is a process, which includes the removal of solvent from a frozen suspension or solution of drug with structure forming additives. Freeze-drying of drug along with additives imparts glossy amorphous structure resulting in highly porous and light weight product. The resulting tablet has rapid disintegration and dissolution when placed on the tongue and the freeze-dried unit dissolves instantly to release the drug. However, the MDTs formed by lyophilization have low mechanical strength, poor stability at higher temperature, and humidity. Along with above complications and its expensive equipment for freeze-drying is observed to be limitation of this technology.

Cotton Candy Process

This process is so named as it utilizes a unique spinning mechanism to produce floss-like crystalline structure, which mimic cotton candy. Cotton candy\ process involves formation of matrix of polysaccharides or saccharides by simultaneous action of flash melting and spinning. The matrix formed is partially recrystallized to have improved flow properties and compressibility. This candy floss matrix is then milled and blended with active ingredients subsequently compressed to Fast dissolving tablets. This process can accommodate high doses of drug and offers improved mechanical strength. However, high-process temperature limits the use of this process.

Molding

Molding process includes moistening, dissolving or dispersing the drug with a solvent then molding the moist mixture into tablets (compression molding with lower pressure than conventional tablet compression), evaporating the solvent from drug solution, or suspension at ambient pressure (no vacuum lyophilization), respectively. The molded tablets formed by compression molding are air-dried. As the compression force employed is lower than conventional tablets, the molded tablet results in highly porous structure, which increases the disintegration and dissolution rate of the product. However, to further improve dissolution rate of the product powder mixture should be sieved through very fine screen.As molding process is employed usually with soluble ingredients (saccharides) which offers improved mouth feel and disintegration of tablets. However, molded tablets have low mechanical strength, which results in erosion and breakage during handling.

Sublimation

The presence of a highly porous structure in the tablet matrix is the key factor for rapid disintegration of Mouth dissolving tablets. Even though the conventional tablets contain highly water-soluble ingredients, they often fail to disintegrate rapidly because of low porosity. To improve the porosity, volatile substances such as camphor can be used in tableting process, which sublimated from the formed tablets, Koizumi et al. developed Mouth dissolving tablet (MDT) utilizing camphor; a subliming material that is removed from compressed tablets prepared using a mixture of mannitol and camphor. Camphor was sublimated in vacuum at 80° for 30 minutes after preparation of tablets [8].

Spray-Drying

Highly porous, fine powders are obtained by this method. Allen et al. utilized this process for preparing Mouth dissolving tablets. The Mouth dissolving tablet formulations consisted of hydrolyzed/unhydrolyzed gelatin as supporting agents for matrix, mannitol as bulking agent, and sodium starch glycolate or croscarmellose sodium as disintegrating agent. Disintegration and dissolution were further improved by adding effervescent components, i.e. citric acid (an acid) and sodium bicarbonate (an alkali). The formulation was spray dried to yield a porous powder. The Mouth dissolving tablets made from this method disintegrated within a minute.

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 [9].

Direct Compression

Easiest way to manufacture tablets is direct compression. Low manufacturing cost, conventional equipment's and limited number of processing steps led this technique to be a preferable one. However disintegration and dissolution of directly compressed tablets depend on single or combined effect of disintegrant, water soluble excipients and effervescing agents. It is essential to choose a suitable and an optimum concentration of disintegrant to ensure quick disintegration and dissolution. Superdisintegrants are newer substances which are more effective at lower concentrations with greater disintegrating efficiency and mechanical strength. On contact with water the superdisintegrants swell, hydrate, change volume or form and produce a disruptive change in the tablet. Effective superdisintegrants provide improved compressibility, compatibility and have no negative impact on the mechanical strength of formulations containing high dose drugs. The type of disintegrants and its proportion are of prime importance. Also factors to be considered are particle size distribution, contact angle, pore size distribution and water absorption capacity. Studies revealed that the water insoluble superdisintegrants like sodium starch glycolate and Croscarmellose sodium show better disintegration property than the slightly water soluble agents like Crospovidone, since they do not have a tendency to swell. Superdisintegrants that tend to swell show slight retardation of the disintegration property due to formation of viscous barrier. There is no particular upper limit regarding the amount of superdisintegrant as long as the mechanical properties of the tablet are compatible with its intended use. The superdisintegrant may be used alone or in combination with other superdisintegrants [10].

PATENTED TECHNOLOGIES

Zydis Technology

This technology includes physical trapping of the drug in a matrix composed of a saccharide and a polymer. Polymers generally employed are partially hydrolyzed gelatin, hydrolyzed dextran, dextrin, alginates, polyvinyl alcohol, polyvinyl pyrrolidine, acacia and mixture of these. The methodology involves solution or dispersion of components is prepared and filled in to blister cavities, which are frozen in a liquid nitrogen environment. The frozen solvent is removed or sublimed to produce porous wafers. Peelable backing foil is used to pack Zydis units. Zydis formulation is sensitive to moisture and may degrade at humidity greater than 65% RH.

Durasolv Technology

The tablets produced by this technology utilize

the conventional tableting equipment. Tablets in this are formulated by using drug, nondirect compression fillers and lubricants. Nondirect compressible fillers are dextrose, mannitol, sorbitol, lactose and sucrose, which have advantages of quick dissolution and avoid gritty texture, which is generally present in direct compressible sugar. The tablets obtained are strong and can be packed in conventional packing in bottles and blisters. Nondirect compressible fillers generally used in the range of 60-95%, lubricant in 1-2.5%.

Orasolv Technology

This includes use of effervescent disintegrating agents compressed with low pressure to produce the Mouth dissolving tablets (MDT). The evolution of carbon dioxide from the tablet produces fizzing sensation, which is a positive organoleptic property. Concentration of effervescent mixture usually employed is 20-25% of tablet weight. As tablets are prepared at low compression force, they are soft and fragile in nature. This initiated to develop Paksolv a special packaging to protect tablets from breaking during storage and transport. Paksolv is a dome-shaped blister package, which prevents vertical movement of tablet with in the depression. Paksolv offers moisture, light and child resistance packing.

Nanocrystal Technology

Nanocrystal technology includes lyophilization of colloidal dispersions of drug substance and water-soluble ingredients filled into blister pockets. This method avoids manufacturing process such as granulation, blending, and tableting, which is more advantageous for highly potent and hazardous drugs. As manufacturing losses are negligible, this process is useful for small quantities of drug.

Dispersible tablet Technology

It offers development of Mouth dissolving tablets with improved dissolution rate by incorporating 8-10% of organic acids and disintegrating agents. Disintegrating agents facilitates rapid swelling and good wetting capabilities to the tablets that results in quick disintegration. Disintegrants include starch, modified starches, microcrystalline cellulose, alginic acid, cross-linked sodium carboxy methyl cellulose and cyclodextrins. Combination of disintegrants improved disintegration of tablets usually less than 1 minute.

Wowtab Technology

"WOW" means without water. This technology utilizes conventional granulation and tableting methods to produce Mouth dissolving tablets employing low and high moldability saccharides. Low moldability saccharides are lactose mannitol, glucose, sucrose and xylitol. High-moldability saccharides are maltose, maltitol, sorbitol and oligosaccharides. When these low and high moldable saccharides used alone tablets obtained do not have desired properties of rapid disintegration and hardness, so combinations are used. This technology involves granulation of low moldable saccharides with high moldable saccharides as a binder and compressing into tablets followed by moisture treatment. Thus tablets obtained showed adequate hardness and rapid disintegration.

Flashtab Technology

This technology includes granulation of excipients by wet or dry granulation method and followed by compressing into tablets. Excipients used in this technology are of two types. Disintegrating agents include reticulated polyvinylpyrrolidine or carboxy methylcellulose. Swelling agents include carboxy methylcellulose, starch, modified starch, microcrystalline cellulose, carboxy methylated starch, etc. These tablets have satisfactory physical resistance. Disintegration time is within 1 minute.

Lyoc Technology

Oil in water emulsion is prepared and placed directly into blister cavities followed by freeze-drying. Non homogeneity during freeze drying is avoided by incorporating inert filler to increase the viscosity finally the sedimentation. High proportion of filler reduces porosity of tablets due to which disintegration is lowered.

Frosta Technology

It utilizes the concept of formulating plastic granules and compressing at low pressure to produce strong tablets with high porosity. Plastic granules composed of:

- Porous and plastic material,
- Water penetration enhancer, and
- Binder.

The process involves usually mixing the porous plastic material with water penetration enhancer and followed by granulating with binder. The tablets obtained have excellent hardness and rapid disintegration time ranging from 15 to 30 s depending on size of tablet.

OraQuick

The OraQuick Mouth -dissolving/disintegrating tablet formulation utilizes a patented taste masking technology. KV Pharmaceutical claims its microsphere technology known as MicroMask, has superior mouth feel over taste-masking alternatives. The taste masking process does not utilize solvents of any kind and therefore leads to faster and more efficient production. Also, lower heat of production than alternative fast-dissolving/disintegrating technologies makes OraQuick appropriate for heat-sensitive drugs. KV Pharmaceutical also claims that the matrix that surrounds and protects the drug powder in microencapsulated particles is more pliable, meaning

tablets can be compressed to achieve significant mechanical strength without disrupting taste-masking. OraQuick claims quick dissolution in a matter of seconds, with good taste-masking. There are no products using the OraQuick technology currently on the market, but KV Pharmaceutical has products in development such as analgesics, scheduled drugs, cough and cold, psychotropics, and anti-infectives considered ideal for MDT formulations [11].

EVALUATION OF MOUTH DISINTEGRATING TABLETS

General Appearance

The general appearance of a tablet, its visual identity and over all "elegance" is essential for consumer acceptance and tablet's size, shape, colour, presence or absence of an odour, taste, surface texture, physical flaws and consistency and legibility of any identifying marking.

Size and Shape

The size and shape of the tablet can be dimensionally described, monitored and controlled.

Tablet thickness

Tablet thickness is an important characteristic in reproducing appearance and also in counting by using filling equipment. Some filling equipment utilizes the uniform thickness of the tablets as a counting mechanism. Ten tablets are taken and their thickness is recorded using micrometer.

Weight variation

20 tablets are selected randomly from the lot and are weighed individually to check for weight variation. Weight variation specification as per I.P. is shown in following table.

Hardness

Hardness of tablet is defined as the force applied across the diameter of the tablet in the order to break the tablet. The resistance of the tablet to chipping, abrasion or breakage under condition of storage transformation and handling before usage depends on its hardness. Hardness of the tablet of each formulation is determined using Monsanto Hardness tester.

Friability (F)

Friability of the tablet determined using Roche friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at height of 6 inches in each revolution. Pre -weighted sample of tablets is placed in the friabilator and are subjected to the 100 revolutions. The friability (F) is given by the formula.

$$F = \frac{W_{int.} - W_{fin}}{W_{int.}}$$

Where, Wint - Weight of tablets before friability.
Wfin - Weight of tablets after friability.

Wetting time

Wetting time of dosage form is related to the contact angle. It needs to be assessed to give an insight into the disintegration properties of the tablets; a lower wetting time implies a quicker disintegration of the tablet. For this purpose, a tablet is placed on a piece of tissue paper folded twice and kept in a small Petri dish (ID = 6.5 cm) containing 6 ml of water, and the time for complete wetting is measured [12]

Water absorption Ratio

A piece of tissue paper folded twice is placed in a small Petridish containing 6 ml of water. A tablet was put on the paper & the time required for complete wetting is measured. The wetted tablet is then weighed. Water absorption ratio, R, is determined using following equation,

- $R = 10 (wa/wb)$

Where, wa is weight of tablet before water absorption & wb is weight of tablet after water absorption.

In vitro dispersion time

In vitro dispersion time is measured by dropping a tablet in a beaker containing 50 ml of Sorenson's buffer pH 6.8. Three tablets from each formulation are randomly selected and in vitro dispersion time is performed.

In vitro Dissolution test

The development of dissolution methods for MDTs is comparable to the approach taken for conventional tablets and is practically identical. Dissolution conditions for drugs which are listed in a pharmacopoeia monograph, is a good place to start with scouting runs for a bioequivalent MDT. Other media such as 0.1 M HCl and buffer (pH 4.5 and 6.8) should be evaluated for MDT much in the same way as their ordinary tablet counterparts. It has been suggested that USP 2 paddle apparatus is the most suitable and common choice for orally disintegrating tablets, with a paddle speed of 50 rpm commonly used.

Stability testing of drug (temperature dependent stability studies): The Mouth disintegrating tablets are packed in suitable packaging and stored under the following conditions for a period as prescribed by ICH guidelines for accelerated studies.

1. 40 ± 1 °C
2. 50 ± 1°c
3. 37 ±1 ° C and RH 75% ± 5%

The tablets are withdrawn after a period of 15 days and analyzed for physical characterization (Visual

defects, Hardness, Friability, Disintegrations and Dissolution etc.) and drug content. The data obtained is fitted into first order equations to determine the kinetics of degradation. Accelerated stability data are plotted according to Arrhenius equation to determine the shelf life at 25°C.

Packaging

Packing is one of the important aspects in manufacturing FDT. The products obtained by various technologies vary in some of the parameters especially in mechanical strength to a good extent. The products obtained from lyophilization process including various technologies such as Zydis, Lyoc, Quicksolv, and Nanocrystal are porous in nature, have less physical resistance, sensitive to moisture, and may degrade at higher humidity conditions. For the above reasons products obtained require special packing. Zydis units are generally packed with peelable backing foil. Paksolv is a special packaging unit, which has a dome-shaped blister, which prevents vertical movement of tablet within the depression and protect tablets from breaking during storage and transport, which is used for Orasolv tablet. Some of the products obtained from Durasolv. WOW Tab, Pharmaburst oraquick, Ziplets, etc. technologies have sufficient mechanical strength to withstand transport and handling shock so they are generally packed in push through blisters or in bottles [13].

Fig 1. Disintegration of tablet by wicking and swelling

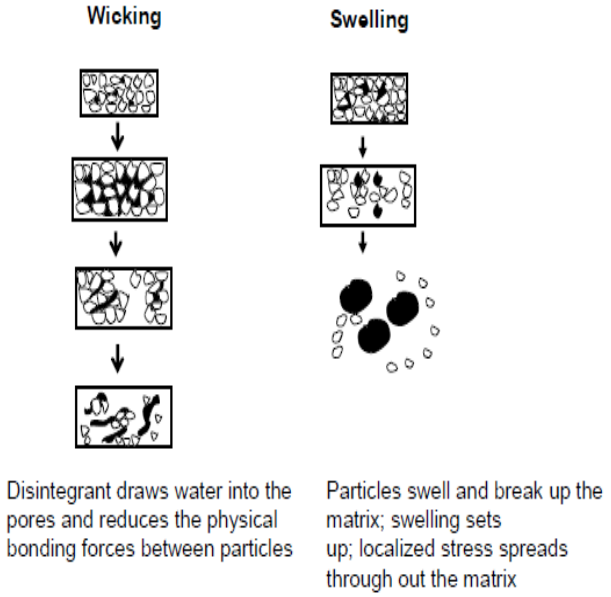


Fig 2. Disintegration by deformation and repulsion

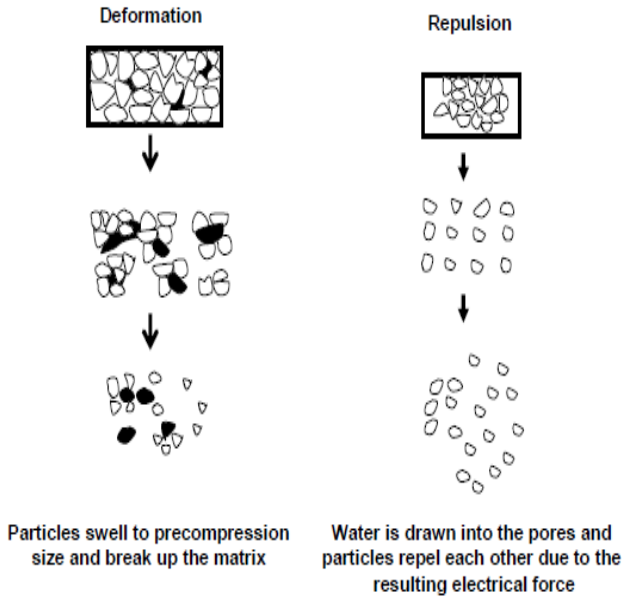
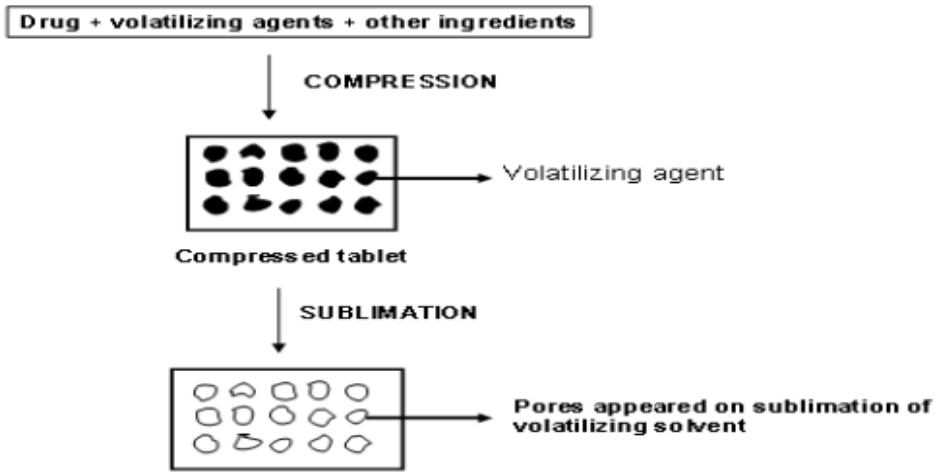


Fig 3. Step Involved In Sublimation Process



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