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A DETAILED STUDY OF MOUTH DISSOLVING DRUG DELIVERY SYSTEM

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ABSTRACT

Patient compliance is one of the most important aspects in the pharmacy practice. In the pharmaceutical industry Oral delivery is currently regarded as the gold standard as it is safest, most convenient and most economical method of drug delivery having the highest patient compliance mouth dissolving drug delivery systems (MDDDS) take an important position in the market by overcoming previously encountered administration problems. Fast disintegrating tablets (FDTs) have received ever-increasing demand during the last decade, and Mouth Dissolving Tablets (MDT) are one of the fruitful results of these technological advancements.

Upon introduction into the mouth, these FDT or MDT tablets dissolve or disintegrate in the mouth in the absence of additional water for easy administration of active pharmaceutical ingredients. A variety of drugs can be administered in the form of MD tablets as they give the advantage of the liquid medication in the solid preparation. Fast- or mouth dissolving tablets have been formulated for pediatric, geriatric, and bedridden patients and for active patients who are busy and traveling and may not have access to water.

Technologies used for manufacturing of orally disintegrating tablets are either conventional technologies or patented technologies. In conventional freeze drying, tablet molding, sublimation, spray drying etc. and in patented tecnology such as Zydis, Orasolv, Durasolv, Wowtab and Flashdose technology are important. Important ingredients that are used in the formulation of ODTs should allow quick release of the drug, resulting in faster dissolution. This review describes the various formulation aspects, disintegrants employed and technologies developed for FDTs, patent formulation, evaluation tests, and marketed formulations.

Key words: Fast Dissolving tablet (MDT), Desired Characteristics, Taste making, Manufacturing technology, Evaluation.

INTRODUCTION

Oral administration is the most popular route for systemic effects due to its ease of ingestion, pain, avoidance, versatility and most importantly, patient compliance. Many patients find it difficult to swallow tablets and hard gelatin capsules and do not take their medicines as prescribed. Many patients have difficulty swallowing (dysphagia) tablets and hard gelatin capsules and consequently do not take medications as prescribed. The difficulty experienced in particular by pediatrics and geriatrics patients, but this also applies to the patients who are ill in bed or traveling. Other groups that may experience problems using conventional oral dosage form include the mentally ill, developmentally disable and patients who are uncooperative. It is

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estimated that 50% of the population is affected by this problem, which results in a high incidence of noncompliance and ineffective therapy. For this reasons, tablets that can dissolve or disintegrate in oral cavity, have attracted a great deal of attention[1]. Indeed, the mouth dissolving tablet is an important and attractive alternative to liquid dosage form. Mouth dissolving tablets are not only indicated for people having difficulty in swallowing but also ideal for unfavorable conditions of administration where water is not available. Syrups are best for pediatrics but they are bulky and drugs are not as stable in liquid form as in solid form like tablets.

Mouth dissolving tablets are also known as fast dissolving, rapid-dissolve, rapimelt, fast melts, porous tablets, EFVDAS or Effervescent Drug Absorption system (Elan Corporation), Orosolv (Cima Labs Inc., USA), Zydis (R. P. Scherer, UK) etc. In order to allow fast disintegrating tablets to dissolve in the mouth, they are made of very porous and soft molded matrices or compressed into tablets with very low compression force[2,3].

Taste-masking is of critical importance in the formulation of an acceptable FDDT. Traditional tablet formulations generally do not address the issue of taste masking, because it is assumed that the dosage form will not dissolve until passing the oral cavity. To eliminate the bitterness of the tablet by adding flavors and sweetening agent or by sugar coating on the tablets. Most of the FDDT technologies incorporate unique forms of taste masking as well[4].

To increase the tablet disintegration, super-disintegrants are added in it, which are very helpful to increase the bioavailability of tablet and to increase the disintegration property of tablet in saliva. Disintegrants are mainly added in the tablets by three methods. These methods are extra- granular, intra-granular and partially extra-granular and intra-granular method. Time for MDT disintegration is normally assumed to be less than 1 min.

The patients can feel the normal disintegration time of MDT from 5-30 sec. MDT's are mainly prepared by various methods like direct compression, wet granulation, solid dispersion and tablet molding etc. Direct compression method is the most widely used and easiest or cost effective method for MDT as compared to other methods.

To ensure the tablet's fast dissolving attribute, water must quickly egress into the tablet matrix to cause rapid disintegration and instantaneous dissolution of the tablet. Maximizing the porous structure of the tablet matrix and incorporating an appropriate disintegrating agents or highly water soluble excipients in the tablet formulation are the basic approaches used in current fast dissolving tablet technologies. Basically, the disintegrant's major function is to oppose the efficacy of the tablet binder and the physical forces that act under compression to form the tablet. The mechanism by which tablet is broken down into smaller particles and then produces a homogeneous suspension or solution is based on: (i) Capillary action (ii) High swellabilty of disintegrants (iii) Capillary action and high swellability (iv) Chemical reaction (Release of Gases)

Recent market studies indicate that more than half of the patient population prefers ODTs to other dosage forms and most consumers would ask their doctors for ODTs (70%), purchase ODTs (70%), or prefer ODTs to regular tablets or liquids (> 80%)[1,5].

Ideal properties of MDT

(i) A MDT should be dissolve or disintegrate in the mouth (in saliva) within seconds.

(ii) It should not require any liquid or water to show its action[6,7].

(iii) Be compatible with taste masking and Have a pleasing mouth feel.

(iv) Be portable without fragility concern.

(v) The excipients should have high wettability, and the tablet structure should also have a highly porous network.

(vi) It should not leave Leave minimal or no residue in the mouth after oral administration of the tablet.

(vii) It should be less effective by environmental conditions like humidity, temperature etc.

(viii) More rapid drug absorption from the pre-gastric area i.e. mouth, pharynx and oesophagus which may produce rapid onset of action[8,9].

(ix) Be adaptable and amenable to existing processing and packaging machinery.

(x) Allow the manufacture of tablets using conventional processing and packaging Equipments at low cost.[10]

(xi) Allow high drug loading

(xii) Have sufficient strength to withstand the rigors of the manufacturing process and post manufacturing handling.

Limitations of mouth dissolving tablets[11-13]

The tablets usually have insufficient mechanical strength. So, careful handling is required.

The tablets may leave unpleasant taste and/or grittiness in mouth if not formulated properly.

Drugs with relatively larger doses are difficult to formulate into MDT e.g. antibiotics like amoxicillin 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.

Difficulties with existing oral dosage form[14]

(i) Patient may suffer from tremors therefore they have difficulty to take powder and liquids. In dysphasia physical obstacles and adherence to an esophagus may cause gastrointestinal ulceration.

(ii) 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.

(iii) Liquid medicaments (suspension and emulsion) are packed in multi-dose container; therefore achievement of uniformity in the content of each dose may be difficult.

(iv) Buccal and sublingual formation may cause irritation to oral mucosa, so patients refused to use such medications.

(v) Cost of products is main factor as parenteral formulations are most costly and discomfort.

Salient feature of fast dissolving drug delivery system[15]

(i) Ease of Administration to the patient who can not swallow.

(ii) No need of water to swallow the dosage form.

(iii) Rapid dissolution and absorption of the drug, which will produce quick onset of action.

(iv) Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach (pregastric absorption). In such cases bioavailability of drug is increased and improves clinical performance through a reduction of unwanted effects.

(v) Good mouth feel property.

(vi) The risk of chocking or suffocation during oral administration of conventional formulation due to physical obstruction is avoided.

(vii) Beneficial in cases such as motion sickness, sudden episodes of allergic attack or coughing, where an ultra rapid onset of action required.

(viii) An increased bioavailability, particularly in cases of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution of these tablets.

(ix) Benefit of liquid medication in the form of solid preparation.

(x) Pre-gastric absorption can result in improved bioavailability, reduced dose and improved clinical performance by reducing side effects.

(xi) Pregastric drug absorption avoids the first-pass metabolism; the drug dose can be reduced if a significant amount of the drug is lost through thehepatic metabolism.[15]

(xii) Rapid drug therapy intervention.

(xiii) New business opportunities: product differentiation, line extension and life-cycle management, exclusivity of product promotion and patent-life extension[16].

Criteria for drug selection

(i) It should not have bitter taste.

(ii) The dose should be less than 20 mg.

(iii) Molecular weight should be small to Moderate.

(iv) Should be of good solubility in water and saliva.

(v) It should have Partially non ionized at the oral cavities pH.

(vi) It should have ability to diffuse and partition into the epithelium of the upper GIT (logp > 1, or preferably > 2)

(vii) Should have extensive First pass metabolism.

(viii) Should have oral tissue permeability.

Challenges in the formulation of ODT[17]

Mechanical strength and disintegration time: Disintegration time will be delayed if the mechanical strength is strong. So a good compromise between these two parameters is always essential.

Taste masking: Effective taste masking of the bitter drugs must be done so that the taste of the drug is not felt in the oral cavity.

Mouth feel: The particles generated after disintegration of the MDT should be as small as possible. ODT should leave minimal or no residue in mouth after oral administration. Moreover addition of flavors and cooling agents like menthol improves the mouth feel.

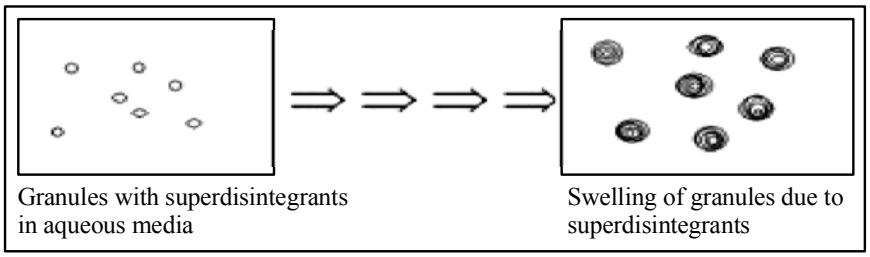
Sensitivity to environmental conditions: ODT generally should exhibit low sensitivity to environment conditions such as humidity and temperature.

Cost: The technology adopted for an MDT should be acceptable in terms of cost of the final product.

In the formulation of FDT the most important additives are as fallows

Superdisintegrants

Fast Dissolving Tablet require faster disintegration, that's why superdisintegrants is needed in formulating FDT/ODT. Superdisintegrant used is the one that effective at low concentration and have greater disintegrating efficiency and they are more effective intragranularly. The problem is, it is hygroscopic therefore not used with moisture sensitive drugs. And this superdisintegrants act by swelling and due to swelling pressure exerted in the outer direction or radial direction, it causes tablet to burst or the accelerated absorption of water leading to an enormous increase in the volume of granules to promote disintegration. Example: croscarmellose sodium, crospovidone, carmellose, carmellose calcium, sodium starch glycolate ion exchange resins (e.g. Indion 414) Sodium starch glycollate has good flowability than crosscarmellose sodium. Cross povidone is fibrous nature and highly compactable.



Mechanism of superdisintegrants by swelling

Swelling index of the superdisintegrants is commonly studied in simulated saliva. Volume occupied by the material at the end of 4 h should be noted and swelling index is calculated by the formula.

Swelling Index = [(Final volume - Initial volume)/initial volume)] x 100

Selecting the superdisintegrant

Although the superdisintegrant primarily affects the rate of disintegration, when used at high levels it can also affect mouth feel, tablet hardness, and friability. Thus, several factors must be considered when selecting a superdisintegrant.

Disintegration

The disintegrant must quickly wick saliva into the tablet to generate the volume expansion and hydrostatic pressures necessary to provide rapid disintegration in the mouth. Compactability. When manufacturing an ODT, it is desirable to have tablets with acceptable hardness at a given compression force

to produce robust tablets that avoid the need to use specialized packaging while maximizing production speed. Thus, a more compactable disintegrant will produce stronger, less-friable tablets.

Mouth feel: To achieve patient compliance, ODTs must provide a palatable experience to the patient. Large particles can result in a gritty feeling in the mouth. Thus, small particles are preferred. If the tablet forms a gel-like consistency on contact with water, however, it produces a gummy texture that many consumers find objectionable.

Flow: As with all direct-compression tablet formulations, attaining good flow and content uniformity is important to achieving the required dosage per unit. In typical tablet formulations, superdisintegrants are used at 2-5 wt. % of the tablet formulation. With ODT formulations, disintegrant levels can be significantly higher. At these higher use levels, the flow properties of the disintegrant are more important because it makes a greater contribution to the flow characteristics of the total blend.

Taste-masking agents

Taste masking of drug may be achieved with preventing the exposure of drug to the tongue through processing or adding competing taste-masking agents. Exposure of solubilized drug to the oral cavity can be prevented by encapsulation in polymer systems or complexation. The approaches are as follows:

- Layering the drug onto inert beads using a binder followed by coating with a taste-masking polymer.
- Granulating the drug and coating with a taste masking polymer.
- Spray drying the drug dispersed or dissolved in a polymeric solution to get taste-masked particles.
- Complexation by the use of inclusion in cyclodextrins.
- Psychological modulation of bitterness.
- Coacervation to form microencapsulated drug within a polymer.
- Formation of pellets by extrusion spheronization.

Sweeteners

Sucrose and other natural sweeteners, such as sorbitol, can be used in effervescent products, although artificial sweetening agents are customary. However, the application of artificial sweeteners is restricted by health regulations. Saccharin or its sodium and calcium salts are used as sweeteners. Aspartame is also employed as a sweetener in effervescent tablets. Earlier, cyclamates and cyclamic acid were the artificial sweeteners of choice, but their use has now been restricted. Some commonly used sweeteners are:

Example: Sorbitol, Mannitol, Maltitol solution, Maltitol, Xylitol, Erythritol, Sucrose, Fructose, Maltose, aspartame, Glycerin, sugars derivatives etc.

Disintegrating agents are substances routinely included in the tablet formulations to aid in the break up of the compacted mass when it is put into a fluid environment. They promote moisture penetration and dispersion of the tablet matrix. These newer substances 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.

Binders

Main role of Binders is to keep the composition of these fast melting tablets together during the compression stage. Binders can either be liquid, semisolid, solid or mixtures of varying molecular weights such as polyethylene glycol. The right selection of a binder or combination of binders is essential to maintain the integrity and stability of the tablet. The temperature of the excipient should be preferably around 30–35^{0}C for faster melting properties. Further, its incorporation imparts smooth texture and disintegration characteristics to the system.

Example: Binders commonly used are cellulosic polymers such as ethylcellulose, hydroxypropylcellulose (HPC), and hydroxypropylmethylcellulose (HPMC), alone or in admixtures povidones, polyvinyl alcohols, and acrylic polymers. Acrylic polymers used are the ammoniomethacrylate copolymer, polyacrylate, and polymethacrylate. Among the cellulosic

Antistatic agent

An antistatic agent is a compound used for treatment of materials or their surfaces in order to reduce or eliminate buildup of static electricity generally caused by the triboelectric effect. An additional thickening agent, generating a stabilized suspension, is added to avoid settling of the particles and moreover provide a pleasant mouth feeling.

Example: colloidal silica (Aerosil), precipitated silica (Sylod.FP244), micronized or non micronized talc, maltodextrins, beta-cyclodextrins, etc. Magnesium stearate, stearic acid, sodium stearylfumarate, micronized polyoxyethylene glycol (micronized Macrogol 6000), leucine, sodium benzoate are used as lubricant[18].

Lubricants

Lubricants remove grittiness and assist in the drug transport mechanism from the mouth down into the stomach. Example: Magnesium stearate, stearic acid, leucine, sodium benzoate, talc, magnesium lauryl sulphate, liquid paraffin etc.

Flavours

Example**:** Peppermint flavour, clove oil, anise oil, eucalyptus oil. Flavoring agents include, vanilla, citrus oils, fruit essences etc.

Fillers

Example: Directly compressible spray dried Mannitol, Sorbitol, xylitol, calcium carbonate, magnesium carbonate, calcium phosphate, pregelatinized starch, magnesium trisilicate, aluminium hydroxide etc.

Surface active agents

Example: sodiumdoecylsulfate, sodiumlaurylsulfate, Tweens, Spans, polyoxyethylene stearate.

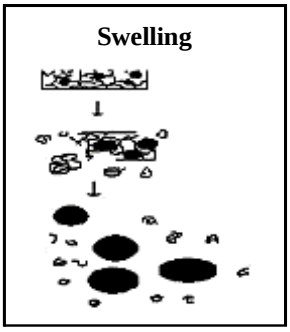
Mechanisms of Super-Disintegrants

There are seven major mechanisms for tablets disintegration as follows

Swelling

Perhaps the most widely accepted general mechanism of action for tablet disintegration is swelling. Swelling is believed to be a mechanism in which certain disintegrating agents (such as starch) impart the

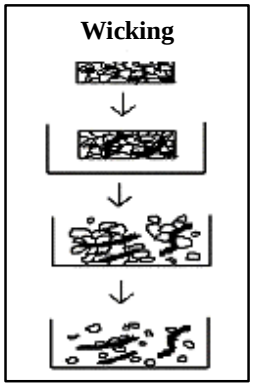
disintegrating effect. By swelling in contact with water, the adhesiveness of other ingredients in a tablet is overcome causing the tablet to fall apart. Tablets with high porosity show poor disintegration due to lack of adequate swelling force. On the other hand, sufficient swelling force is exerted in the tablet with low porosity. It is worthwhile to note that if the packing fraction is very high, fluid is unable to penetrate in the tablet and disintegration is again slows down.



Particles swell and break up the matrix form within

Porosity and capillary action (Wicking)

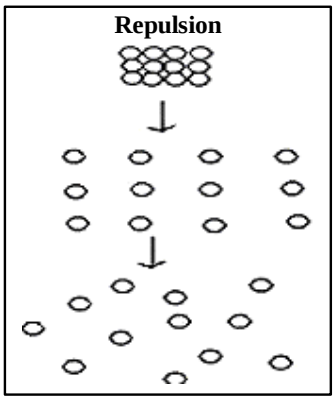
Effective disintegrants that do not swell are believed to impart their disintegrating action through porosity and capillary action. When we put the tablet into suitable aqueous medium, the medium penetrates into the tablet and replaces the air adsorbed on the particles, which weakens the intermolecular bond and breaks the tablet into fine particles. Tablet porosity provides pathways for the penetration of fluid into tablets. The disintegrant particles (with low cohesiveness & compressibility) themselves act to enhance porosity and provide these pathways into the tablet. Water uptake by tablet depends upon hydrophilicity of the drug /excipient and on tableting conditions. For these types of disintegrants maintenance of porous structure and low interfacial tension towards aqueous fluid is necessary which helps in disintegration by creating a hydrophilic network around the drug particles.



Water is pulled by disintegrant and reduced the physical bonding force between particles

Due to disintegrating particle/particle repulsive forces

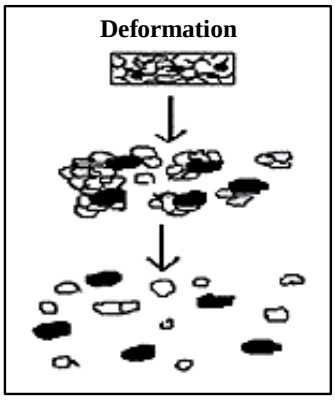
Another mechanism of disintegratn attempts to explain the swelling of tablet made with ‘nonswellable’ disintegrants. Guyot-Hermann and Ringard[53] have proposed a particle repulsion theory based on the observation that nonswelling particle also cause disintegration of tablets. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it. Researchers found that repulsion is secondary to wicking.



Water is drawn into pores and particles repel each other because of resulting electrical force

Due to deformation

During tablet compression, disintegranted particles get deformed and these deformed particles get into their normal structure when they come in contact with aqueous media or water. Occasionally, the swelling capacity of starch was improved when granules were extensively deformed during compression. This increase in size of the deformed particles produces a break up of the tablet. Starch grains are generally thought to be "elastic" in nature meaning that grains that are deformed under pressure will return to their original shape when that pressure is removed. But, with the compression forces involved in tableting, these grains are believed to be deformed more permanently and are said to be "energy rich" with this energy being released upon exposure to water.



Particles swell to precompression size and break up matrix

Because of heat of wetting (air expansion)

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

Due to release of gases

Carbon dioxide 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 manufacturing of the tablets. The effervescent blend is either added immediately prior to compression or can be added in to two separate fraction of formulation.

By enzymatic reaction

Here, enzymes presents in the body act as disintegrants. These enzymes destroy the binding action of binder and helps in disintegration

Disintegrating enzymes

Enzymes	Binder
Amylase	Starch
Protease	Gelatin
Cellulase	Cellulose and it's derivatives
Invertase	Sucrose

Taste masking methods[19,20]

(i) The drugs are mostly bitter in nature. Skillful taste masking is needed to hide the bitter taste in ODT formulations. Following methods are used in Taste masking.

(ii) Simple wet granulation method or rollercompaction of other excipients. Spray drying can also employed to shroud the drug.

(iii) Drugs can be sifted twice or thrice in small particle size mesh with excipients such as sweeteners and flavors etc.

(iv) Drug particles are coated directly.

(v) Granulation of the drug with certain excipients followed by the polymer coating.

(vi) If the drug is tasteless or very low dose, direct blend of bulk drug substance into fast disintegrating matrix is straightforward.

(vii) Formation of pellets by extrusion spheronization.

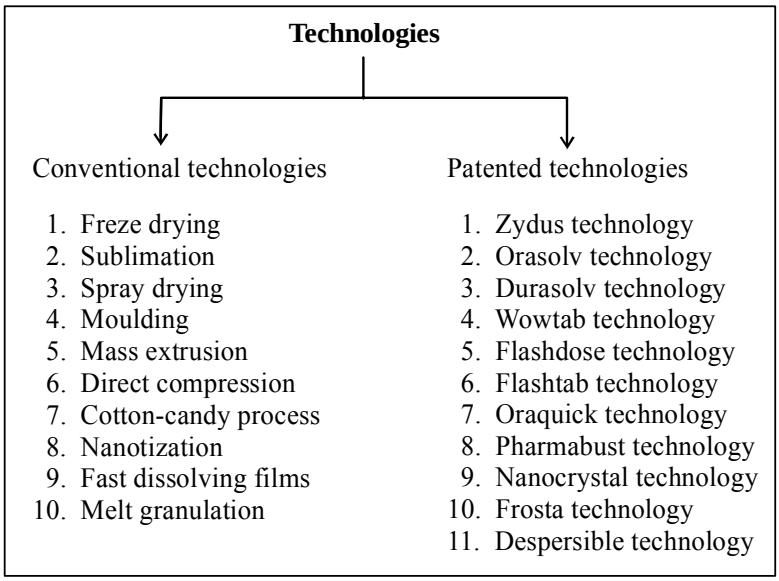
(viii) Coacervation to form microencapsulated drug within a polymer.

(ix) Cyclodextrins can be used to trap or complex, cyclodextrin help to solubilze many drugs.

(x) Drug complexation with resinates are insoluble and no taste in oral cavity. Examples of drugs where this technique has been successfully demonstrated include ranitidine, risperidone and paroxetine.

(xi) Other methods include hot melt and supercritical fluids.

(xii) Adjustment of pH Values: Many drugs are less soluble at pH different from the pH value of the mouth, which is around 5.9. Solubilization inhibitor, such as sodium carbonate, sodium bicarbonate, sodium hydroxide, or calcium carbonate, was added to increase the pH when granules including a drug-sildenafil-dissolved in aqueous medium, the bitter taste of the drug was successfully masked by a sweetener alone.



Orally fast disintegrating tablets

Freeze drying or lyophilisation

A process, in which water is sublimated from the product after freezing, is called freeze drying. Freezedried forms offer more rapid dissolution than other available solid products. Lyophilization can be used to prepare tablets that have very porous open matrix network into which saliva rapidly moves to disintegrate lyophilized mass after it is placed in mouth. Apart from the matrix and active constituents, the final formulation may contain other excipients, which improve the process characteristics or enhance the quality of final product. These include suspending agents, wetting agents, preservatives, antioxidants, colors and flavors. The preferred drug characteristics for freeze drying formulations are water insoluble, low dose, chemically stable, small particle size and tasteless.

Advantage

Pharmaceutical substances can be processed at non elevated temperature, thereby eliminating adverse thermal effects.

Disadvantage

(i) Due to high cost of equipments Lyophilization is relatively expensive and time consuming manufacturing process.

(ii) Fragility, which make the use of conventional packing difficult and poor stability during storage under stressful condition[21,22].

Sublimation

This process involves addition of some inert volatile substances like urea, urethane, naphthalene, camphor, etc to other excipients and the compression of blend into tablet. Removal of volatile material by sublimation creates pores in tablet structure, due to which tablet dissolves when comes in contact with saliva. Additionally several solvents like cyclohexane, benzene etc can also be used as pore forming agents. Orodispersable Tablets with highly porous structure and good mechanical strength have been developed by this method.

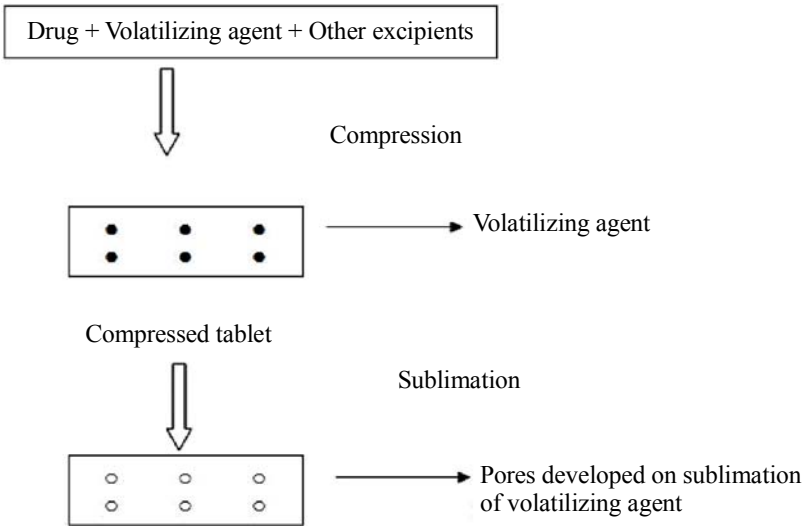


Fig. 1: Steps Involved in sublimation

Spray drying

A highly porous and fine powder is prepared by spray drying an aqueous composition containing support matrix and other components. This is then mixed with active ingredient and compressed into tablet.

The formulations contained hydrolyzed and unhydrolyzed gelatin as a supporting agent for the matrix, mannitol as a bulking agent and sodium starch glycolate/croscaramellose as a disintegrant. Disintegration and dissolution were further enhanced by adding an acid (e.g. citric acid) or an alkali (e.g., sodium bicarbonate). The suspension of above excipients was spray-dried to yield a porous powder which was compressed into tablets. Tablets manufactured by this method disintegrated in < 20 sec. in an aqueous medium[23].

Moulding

Molded tablets are prepared by using watersoluble ingredients so that the tablets dissolve completely and rapidly. The powder blend is moistened with a hydro-alcoholic solvent and is molded into tablets under pressure lower than that used in conventional tablet compression. The solvent is then removed by air drying.

Advantage

(i) Moulded tablets posess porous structure, which facilitates rapid disintegration and easy dissolution.

(ii) Moulded tablets offer improved taste due to water-soluble sugars present in dispersion matrix.

Disadvantage

But moulded tablets lack good mechanical strength and can undergo breakage or erosion during handling and opening of blister packs[24]. However, adding sucrose, acacia or polyvinyl pyrrolidone can increase mechanical strength.

Different moulding techniques can be used to prepare mouth-dissolving tablets:

Compression moulding: The powder mixture previously wetted with a solvent ike ethanol/water is compressed into mould plates to form a wetted mass.

Heat moulding: A molten matrix in which drug is dissolved or dispersed can be directly moulded into Orodispersable Tablets.

No vacuum lyophilization: This process involves evaporation of solvent from a drug solution or suspention at a standard pressure.

Mass extrusion[25,26]

In this technique, a blend of active drug and other ingredients is softened using solvent mixture of water soluble polyethylene glycol, using methanol and then the softened mass is extruded through the extruder or syringe to get a cylinder of product, which is finally cut into even segments with the help of heated blades to get tablets. The dried cylinder can be used to coat the granules of bitter tasting drugs and there by masking their bitter taste.

Direct compression

The disintegrant addition technology (direct compression) is the most preferred technique to manufacture the tablets. Advantages:

(i) High doses can be accommodated and final weight of the tablet can exceed that of other methods.

(ii) Easiest way to manufacture the MDT tablets.

(iii) Conventional equipment and commonly available excipients are used.

(iv) A limited number of processing steps are involved.

(v) Cost-effectiveness.

Tablet size and hardness strongly affect the disintegrant efficacy. Hard and large tablets have more disintegration time than normally required. Very soft and small tablets have low mechanical strength. So, an optimum kind and concentration of disintegrant should be chosen to achieve quick disintegration and high dissolution rates. Above the critical oncentration level, however, disintegration time remains approximately constant or even increases.

Cotton-candy process

In this process Shearform technology is used in the preparation of a matrix known as FLOSS, made from the combination of the recipients either alone or with the drugs. The fibrous nature of the floss is similar to the cotton-candy fibers. The floss is commonly made of saccharides such as sucrose, dextrose, lactose and fructose at temperatures ranging between 180-266 °F. Other polysaccharides such as polymaltodextrins and polydextrose can be transformed into fibers at 30-40% lower temperature range.

Nanonization[27]

In this process, the particles of the drug are reduced in size to nanoparticles by milling the drug in the proprietary wet milling process. The agglomeration can be prevented by surface adsorption of the nanocrystals. These are then compressed and changed into a tablet. This technique is very useful for less water soluble drugs. The bioavailability of the drug is increased as the disintegration time is reduced to a significant extent.

Fast dissolving films

In this technique, a non-aqueous solution is prepared containing water soluble film forming polymers (carboxy methylcellulose, hydroxypropyl methylcellulose, hydroxyl ethylcellulose, hydroxyl

propylcellulose etc.), drug and other taste masking ingredients, which is allowed to form a film after evaporation of solvent [28].

In case of a bitter drug, resin adsorbate or coated microparticles of the drug can be incorporated into the film[29]. This film, when placed in mouth, melts or dissolves rapidly, releasing the drug in solution or suspension form.

Melt granulation

Abdelbary et al.[54] prepared ODT by incorporating a hydrophilic waxy binder (super polystate) PEG-6- Sterate. Superpolystate is a waxy material with an melting point of 33-37^{0}C. It is not only acts as a binder and increases the physical resistance of tablets, but also helps the disintegration of tablets as it melts in the mouth and solubilizes rapidly leaving no residue.

Advantages

(i) Neither solvent nor water used in this process.

(ii) Fewer processing steps needed thus time consuming drying steps eliminated.

(iii) There are no requirements on the compressibility of active ingredients and the entire procedure simple, continuous and efficient.

(iv) Uniform dispersion of fine particle occurs.

(v) Good stability at varying pH and moisture levels.

Disadvantages

(i) Requires high energy input.

(ii) The melt technique is that the process cannot be applied to heat-sensitive materials owing to the elevated temperatures involved.

(iii) lower-melting-point binder risks situations where melting or softening of the binder occurs during handling and storage of the agglomerates

(iv) Higher-melting-point binders require high melting temperatures and can contribute to instability problems especially for heat-labile materials.

Table 1: Comparison of technologies for preparing FDTs

Technology	Advantages	Disadvantages
Freeze drying	Immediate dissolution (2-10 s)	Very poor physical resistance high cost of production sensitive to humidity low dose of water-soluble drugs
Tableting (sublimation)	Good physical resistance	Harmful residual adjuvants extra equipments for heating not applicable to volatile and heat sensitive drugs
Molding	Very rapid dissolution (5–15 s)	High cost of production
	High dose	Weak mechanical strength possible limitations in stability

Cont…

Technology	Advantages	Disadvantages
Tableting (standard)	Low cost of production use of standard equipment/materials high dose good physical resistance	Signifi cant effects of the size and hardness of the tablets on disintegration property
Tableting (effervescent)	Use of standard equipment high dose good physical resistance pleasant effervescent mouth feel	Operating in controlled low humidity need of totally impermeable blister
Tableting (Humidity treatment)	Good physical resistance pleasant mouth feel	Extra equipments for humidification and drying possible limitations in stability high cost of production not suitable for moisture sensitive compounds fragile before humidity treatment

Patented technologies for MDT's: The main patented technologies for mouth dissolving tablets are as follows :

Zydis Tecnology

Zydis formulation is a unique freeze dried tablet in which drug is physically entrapped or dissolved within the matrix of fast-dissolving carrier material. When Zydis units are put into the mouth, the freeze-dried structure disintegrates instantaneously and does not require water to aid swallowing. The Zydis matrix is composed of many materials designed to achieve a number of objectives. To impart strength and resilience during handling, polymers such as gelatin, dextran or alginates are incorporated. These form a glossy amorphous structure, which imparts strength. To obtain crystallinity, elegance and hardness, saccharides such as Mannitol or sorbitol are incorporated. Water is used in the manufacturing process to ensure production of porous units to achieve rapid disintegration. Various gums are used to prevent sedimentation of dispersed drug particles in the manufacturing process. Collapse protectants such as glycine prevent the shrinkage of Zydis units during freeze drying process or long term storage. Zydis products are packed in blister packs to protect the formulation from moisture in the environment.

Limitations

- The amount of drug could be incorporated should generally be less than 400 mg for insoluble drugs and less that 60 mg for soluble drugs.
- The particle size of the insoluble drugs should not be less than 50 μm and not more than 200 μm to prevent sedimentation during processing.

Advantages

- Buccal pharyngeal and gastric regions are all areas of absorption from this formulation. Any pre-gastric absorption avoids first-pass metabolism and can be an advantage in drugs that undergo a great deal of hepatic metabolism.
- The Zydis formulation self-preserving because the final water concentration in the freeze-dried product is too low to allow for microbial growth.
- Patients who have difficulty swallowing oral medication due to dysphagia, stroke or medical conditions such as gastroesophageal reflux disease, multiple sclerosis or Parkinson's disease.

- Pediatric patients.
- Patients who refuse or spit out oral medications, including patients with psychiatric or behavioral disorders.
- Companion animals such as dogs and cats.

Disadvantages

- The process of freeze-drying is a relatively expensive manufacturing process.
- The formulation is very lightweight and fragile, and therefore should not be stored in backpacks or the bottom of purses.
- It has poor stability at higher temperatures and humidities.
- The freeze-drying is time consuming process.
- It has poor physical resistance.
- Loading of high dose of water-soluble drugs is not possible.

Orasolv technology[30]

This technology is patented by CIMA Labs. This includes use of effervescent disintegrating agents compressed with low pressure to produce the MDTs. The OraSolv process typically involves blending the microencapsulated API with magnesium oxide and mannitol to aid in the release of the drug from the polymeric coating. These microparticles are further blended with other excipients and loosely compressed to maintain some degree of tablet porosity to aid dispersion. Compression forces need to be kept to a minimum so as not to disrupt the API taste-masking coating. With OraSolv tablet technology, tablets are compressed to a hardness of 6-25 N and packaged in blister cards.

The resultant tablet is relatively weak and friable and requires specific patented packaging technology (PakSolv, CIMA Labs) was developed to protect the tablets from breaking during transport and storage.

The OraSolv ODT technology uses taste-masked drug microparticles in a formulation that enhances tablet disintegration. On contact with saliva, the effervescent system promotes disintegration of the tablet. Carbon dioxide is generated by a reaction of the formulation components upon exposure to water (saliva in the mouth). This causes a sensation in the mouth that is pleasant to the patient and tends to stimulate further saliva roduction, which also aids in disintegration.

Advantages

(i) The OraSolv technology has been used for drug strengths in the range of 1 mg to 750 mg. Depending on formulation and tablet size, the disintegration time of the tablet can be designed in the range of 10 to 40 seconds.

(ii) PakSolvR is a “dome-shaped” blister package that prevents the vertical movement of the tablet within the depressions, because the diameter of the lower portion of the dome is too narrow to accommodate the tablet. PakSolvR also offers light, moisture, and child resistance.

(iii) In addition to the drug and effervescent component, the OraSolv technology uses generally recognized as safe (GRAS) excipients, which may include a filler, disintegrant, flavor, sweetener, lubricant and color.

Disadvantages

Both OraSolv and DuraSolv products are sensitive to moisture due to the presence of the effervescent system and must be packaged appropriately.

Durasolv technology[30]

The DuraSolv technology has a formulation similar to the OraSolv technology, combining tastemasked drug microparticles with or without a low effervescence-containing formulation, was developed by CIMA labs, consist of a drug, fillers and the lubricants. The tablets are prepared by conventional tabletting equipment and have good rigidity. They can be packed in the conventional tabletting equipment and have good rigidity.

Advantages

DuraSolv technology is good for tablets having low amount (125 mcg to 500 mg) of active ingredients and tablets are compressed to a greater hardness of 15-100 N, resulting in a more durable ODT. As a result, this technology enables packaging flexibility; tablets can be bottled and blistered.

Disadvantages

The technology is not compatible with larger doses of active ingredients, because the formulation is subjected to high pressure during compaction. The drug powder coating in Durasolv may become fractured during compaction, exposing the bitter tasting drugs to the patient taste buds[31].

Wowtab technology

Yamanauchi pharmaceutical company patented this technology. ‘wow’ means ‘without water’. The WOW in the WOWTAB signifies the tablet is to be given without water. The active ingredients may constitute upto 50% w/w of the tablet. In this technique, saccharides of both low and high mouldability are used to prepare the granules. Mouldability is the capacity of a compound to be compressed.

This technology utilizes sugarand sugar-like excipients. The two different types of saccharides having high moldability like maltose, mannitol, sorbitol, and oligosaccharides (good binding property) and low moldability like lactose, glucose, mannitol, xylitol (rapid dissolution) are combined to obtain a tablet formulation with adequate hardness and fast dissolution rate. Highly mouldable substance has high compressibility and thus shows slow dissolution. The combination of high and low mouldability is used to produce tablets of adequate hardness[32].

Advantages

(i) The Wowtab product dissolves quickly in 15 s or less.

(ii) Wowtab product can be packed in both into conventional bottle and blister packs.

Flashdose technology

This technology is patented by Fuisz. This system uses the combination of both Shearform and Ceform technologies in order to mask the bitter taste of the drug. A sugar based matrix, called ‘Floss’ is used, which is made up of a combination of excipients (crystalline sugars) alone or in combination with drugs. Nurofen meltlet, a new form of Ibuprofen, as a mouth-dissolving tablet is the first commercial product prepared by this technology and launched by Biovail Corporation.

Drawbacks

(i) The dosage form can accommodate only up to 600 mg of drug.

(ii) Tablets produced are highly friable, soft and moisture sensitive. Therefore specialized packing is required.

Flashtab technology

Prographarm laboratory have a patent over this technology. In this technology, microgranules (i.e., active ingredient in the form of microcrystals) of the taste-masked active drug are used. These may be prepared by using conventional techniques like coacervation, microencapsulation, simple pan coating methods and extrusion-spheronisation. All these processes utilize conventional tabletting technology.[33] These taste-masked micro crystals of active drug, disintegrating agent, such as carboxymethylcellulose or insoluble reticulated polyvinylpyrrolidone; a swelling agent, such as carboxymethylcellulose, starch, modified starch, carboxymethylated starch, microcrystalline cellulose, and possibly directly compressible sugars and other excipients like soluble diluents etc are compressed to form a multiparticulate tablet that disintegrates rapidly. The mixture of excipients is prepared by either dry or wet granulation methods[34].

Oraquick technology

K. V. S. Pharmaceuticals have a patent over this technology[35]. It utilizes taste masking microsphere technology called as micromask, which provides superior mouth feel over taste masking alternatives, significant mechanical strength, and quick disintegration/dissolution of product. Any kind of solvents are not utilized by taste masking process. Therefore it leads to superior and fast efficient production.

Pharmaburst technology

SPI Pharma, New Castle have a patent over this technology. It utilizes the coprocessed excipients to develop MDTs, which dissolves within 30-40 s. This technology involves dry blending of drug, flavour, and lubricant followed by compression into tablets. Tablets obtained have sufficient strength so they can be packed in blister packs and bottles[36].

Nanocrystal technology[37]

Elan, King of Prussia have a patent over this technology. This technology includes Nanocrystal colloidal dispersions of drug substance are combined with water-soluble GRAS (Generally Regarded As Safe) ingredients, filled into blisters, and lyophilized. The resultant wafers are remarkably robust, yet dissolve in very small quantities of water in seconds. This method avoids manufacturing process such as granulation, blending, and tabletting, which is more advantageous for highly potent and hazardous drugs. As manufacturing losses are negligible, this process is useful for small quantities of drug.

Advantages

(i) Pharmacokinetic benefits of orally administered nanoparticles (< 2 microns) in the form of a rapidly disintegrating tablet matrix.

(ii) Cost-effective manufacturing processes that utilize conventional, scalable unit operations.

(iii) Exceptional durability, enabling use of conventional packaging equipment and formats (i.e., bottles and/or blisters).

(iv) Wide range of doses (up to 200 mg of API per unit).

Frosta technology[38]

A new technology called Frosta (Akina) was developed for making FMTs. The Frosta technology utilises the conventional wet granulation process and tablet press for cost-effective production of tablets. The Frosta tablets are mechanically strong with friability of < 1% and are stable in accelerated stability conditions when packaged into a bottle container. They are robust enough to be packaged in multi-tablet vials. Conventional rotary tablet presses can be used for the production of the tablets and no other special instruments are required. Thus, the cost of making FMTs is lower than that of other existing technologies. Depending on the size, Frosta tablets can melt in < 10 s after placing them in the oral cavity for easy swallowing. The Frosta technology is ideal for wide application of FMTs technology to various drug and nutritional formulations.

Dispersible tablet technology[39]

Lek in Yugoslavia have a patent over this technology. Dihydroergotoxine is poorly soluble in water in the free base form. An improved dissolution rate of dihydroergotoxine methanesulphonate was observed with dispersible tablets containing 0.8-10%, preferably about 4% by weight, of an organic acids. One of the essential excipients in the cimetidine formulation was a disintegrating agent. The disintegrating agents include starch or modified starches, microcrystalline cellulose, alginic acid, cross-linked sodium carboxymethyl cellulose, and cyclodextrin polymers. Dihydroergotoxine and cimetidine, which were claimed to disintegrate in less than 1 minute when in contact with water at room temperature.

Table 2: List of patented technologies based branded products

Patented technology	Basis of technology	Technology developed by company	Active ingredient	(Brand names)
Zydis	Lyophilization	R. P. Scherer, Inc.	Loratidine	Claritin reditab and dimetapp quick dissolve
Orasolv	Direct compression	Cima Labs, Inc.	Paracetamol zolmitriptan	(Tempra quicklets), (Zolmig repimelt),
Durasolv	Direct compression	Cima Labs, Inc.	Hyoscyamine sulfate zolmitriptan	(NuLev) (Zolmig ZMT)
Wowtab	Direct compression	Yamanouchi Pharma Tech. Inc.	Famotidine	(Gaster D)
Flashdose	Cotton candy process	Fuisz Technology Ltd.	Tramadol HCl	(Relivia flash dose)
Flashtab	Direct compression	Ethypharm	Ibuprofen	(Nurofen Flash Tab)
Quicksolv	Lyophilization	Janssen pharmaceutics	Cisapride monohydrate risperidone	Propulsid quicksolv risperdal MTab
Lyoc	Lyophilization	Farmalyoc	Phloroglucinol hydrate	Spasfon Lyoc
Ziplets	Direct compression	Eurand International	Ibuprofen	(Cibalgina due fast)
Advatab	Microcaps and diffuscap CR technology	Eurand International	Cetrizine paracetamol	Adva Tab cetrizine, Adva Tab paracetamol
Oraquick	Micromask taste masking	K. V. Pharm. Co., Inc.	Hyoscyamine sulfate ODT	Hyoscyamine sulfate ODT

Preformulation studies fast dissolving tablet[40]

Preformulation study relates to pharmaceutical and analytical investigation carried out proceeding and supporting formulation development efforts of the dosage form of the drug substance. Preformulation yields basic knowledge necessary to develop suitable formulation for the toxicological use. It gives information needed to define the nature of the drug substance and provide frame work for the drug combination with pharmaceutical excipients in the dosage form. Hence, the following preformulation studies were performed on the obtained sample of drug.

Bulk density (Db)

It is the ratio of total mass of powder to the bulk volume of powder. It is expressed in g/ml. This was determined by pouring an accurately weighed quantity of blend into a graduated cylinder and then the volume and weight was measured.

$$Db = M/ Vb$$

Where, Bulk density = Db, Weight of powder = M and Volume of packing = Vb

Tapped density (Dt)

It is the ratio of total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for 750 times and the tapped volume was noted if the difference between these two volumes is less than 2%. If it is more than 2%, tapping is continued for 1250 times and tapped volume was noted. Tapping was continued until the difference between successive volumes is less than 2 % (in a bulk density apparatus). It is expressed in g/mL and is given by $D_t = M / V_t$

Where, M is the mass of powder V_t is the tapped volume of the powder.

Compressibility

The compressibility index (Carr's Index) was determined by using following equation,

$$\text{Carr's Index (\%)} = [(Dt – Db) \times 100] / Dt$$

Where, Dt is the tapped density of the powder and Db is the bulk density of the powder.

Table 3: Relationship between % compressibility and flow ability

% Compressibility	Flow ability
5-12	Excellent
12-16	Good
18-21	Fair passable
23-35	Poor
33-38	Very poor
< 40	Very very poor

Angle of repose (q)

The friction forces in a loose powder can be measured by the angle of repose (q). It is an indicative of the flow properties of the powder. It is defined as maximum angle possible between the surface of the pile of powder and the horizontal plane.

The angle of repose was determined by the funnel method. The accurately weighed powder was taken in a funnel. The height of a funnel was adjusted in such a way that its tip just touches the apex of the heap of the powder. The powder was allowed to flow through funnel freely onto the surface. The diameter of the powder heap was measured and angle of repose was calculated using following equation,

$$\tan(\theta) = h/r$$

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

Where, θ is the angle of repose.h is the height in cms r is the radius in cms.

The powder mixture was allowed to flow through the funnel fixed to a stand at definite height (h). The angle of repose was then calculated by measuring the height and radius of the heap of powder formed. Care was taken to see that the powder particals slip and roll over each other through the sides of the funnel. Relationship between angle of repose and powder flow property.

Table 4: Angle of repose as an indication of powder flow properties

S. No.	Angle of repose (°)	Type of flow
1	< 20	Excellent
2	20-30	Good
3	30-34	Passable
4	> 34	Very poor

Hausner ratio

Hausner ratio is an indirect index of ease of powder flow. Hosner ratio is the ratio of tapped density to bulk density, i.e.,

$$\text{Hausner ratio} = D_t / D_b$$

Where, D_t is the tapped density and D_b is the bulk density. Powder with Housner ratio less than 1.18, 1.19, 1.25, 1.3- 1.5 and greater the 1.5 indicate excellent, good, passable, and very poor, respectively.

Porosity

Percent relative porosity (ε) was obtained using the relationship between apparent density (ρapp) and true density (ρtrue) which is calculated by following formula.

$$\varepsilon = (1 - \rho app / \rho true) \times 100$$

Drug excipient compatibility study

This study was carried out to detect any changes on chemical constitution of the drug after combined it with the excipients. Compatibility of the drug with excipients was determined by FT-IR spectral analysis.

Evaluation of mouth dissolving tablet[41-44]

General appearance

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

Uniformity of weight

20 tablets were selected randomly from the lot and weighted individually to check for weight variation. Weight variation specification as per I.P. is shown in Table 5.

Table 5: Weight variation specification as per IP

Average weight of tablet	% Deviation
80 mg or less	± 10
More than 80 mg but less than 250 mg	± 7.5
250 mg or more	± 5

Hardness

Hardness or tablet crushing strength (fc), the force required to break a tablet in a diametric compression was measured using Monsanto tablet hardness tester. It is expressed in Kg/cm^2.

Friability (F)

Friability is the loss of weight of tablet in the container due to removal of fine particles from the surface. Friability test is carried out to access the ability of the tablet to withstand abrasion in packaging, handling and transport.

Friability of the tablets was determined using Roche friabilitor at 25 rpm/min for 4 min 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 I height of 6 inches in each revolution. Preweighted sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. Tablets were dusted using a soft muslin cloth and reweighed. Twenty tablets were weighed and loss in weight (%) was calculated. The friability (F) is given by the formula,

$$\% \text{ Friability} = [(W_1-W_2)100]/W_1$$

Where, W_1= Weight of tablet before test, W_2 = Weight of tablet after test

Dissolution test

USP 2 Paddle apparatus was used and with a paddle speed of 50 rpm commonly used. Phosphate buffer (pH 6.8) (900 mL) was used as a dissolution medium. Samples were withdrawn at proper interval 0.5 min, 1 min, 2 min…..5 min. and proper sink condition was maintained. The samples were analyzed by generally UV-Spectrophotometer.

Typically, the dissolution of orally disintegrating tablets is very fast when using USP monograph conditions, hence slower paddle speeds may be utilized to obtain a profile. Large tablets approaching or exceeding one gram and containing relatively dense particles may produce a mound in the dissolution vessel, which can be prevented by using higher paddle speeds. These two situations expand the suitable range to 25-75 rpm.

The USP 1 basket apparatus may have certain applications for orally disintegrating tablets, but is used less frequently due to the physical properties of these tablets. Specifically, tablet fragments or disintegrated tablet masses may become trapped on the inside top of the basket at the spindle where little or no effective stirring occurs, yielding irreproducible dissolution profiles.

In vivo disintegration test

The time for disintegration of ODTs is generally < 1 min and actual disintegration time that patience can experience ranges from 5 to 30 s. The standard procedure are that the test was carried out on 6 tablets using the apparatus specified in I.P. -1996 distilled water at 37°C ± 2°C was used as a disintegration media and the time in second is taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured in seconds.

Uniformity of dispersion

Two tablets were kept in 100 mL water and gently stirred for 2 minutes. The dispersion was passed through 22 meshes. The tablets were considered to pass the test if no residue remained on the screen[45].

Mechanical strength

Tablets should possess adequate strength to withstand mechanical shocks of handling in manufacturing, packaging and shipping. Crushing strength and friability are two important parameter to evaluate a tablet for its mechanical strength.

Crushing strength

It is the force required to break a tablet by compression in the radial direction, it is an important parameter in formulation of mouth dissolve tablets because excessive crushing strength significantly reduces the disintegration time.

Wetting time

Wetting time corresponds to the time taken for the tablet to disintegrate when kept motionless on the tongue. Wetting time is closely related to the inner structure of the tablets and to the hydrophilicity of the excipient. The Washburn Equation, (Washburn, 1921), is one of the most common equations for describing liquid penetration into porous solids. It states that the liquid penetration rate is directly proportional to that pore radius and is affected by the hydrophilicity of the powders, the liquid surface tension (i), the cosine of the contact angle θ, and inversely proportional to the liquid viscosity (h).

$$d\,x^2/dt = r¡\cos\theta\,/(2\,h)$$

Where x being the liquid penetration distance, thus x^2 the liquid penetration area, r is the capillary radius, ¡ is the surface tension, h is the liquid viscosity, t is the time, and θ is the contact angle. It is obvious that pores size becomes smaller and wetting time increases with an increase in compression force or a decrease in porosity. A linear relationship exists between wetting time and disintegration time. Thus wetting is the important step for disintegration process to take place. A piece of tissue paper folded double was placed in a Petri plate (internal diameter is 6.5 cm) containing 6 mL of water. The tablet was placed on the paper and the time for complete wetting of the tablet was measured in seconds. The method was slightly modified by maintaining water at 37°C.

Wetting time and water absorption ratio

A piece of tissue paper folded twice was placed in a small culture dish (i.d. = 6.5 cm) containing 6 mL of water[46]. A tablet was placed on the paper, and the time for complete wetting was measured. The wetted tablet was again weighed. Water absorption ratio, *R*, was calculated using the formula;

$R = 100\,(W_a - W_b)\,Wb$ Where, W_a and W_b are the weight after and before water absorption, respectively.

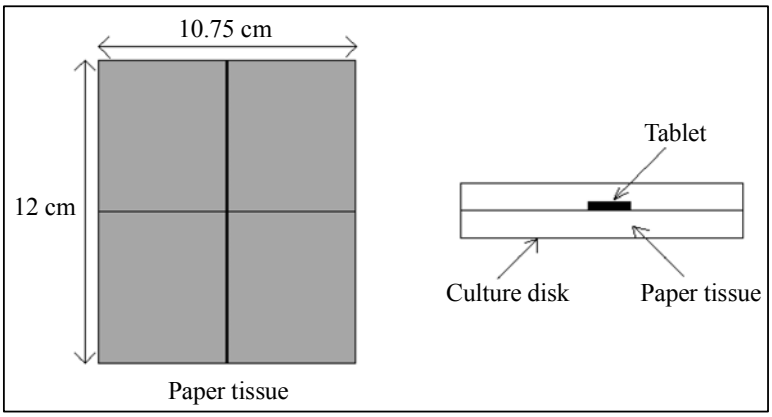


Fig. 1: Schematization measurement of tablet wetting time and water absorption ratio

Identification of drug sample

It was confirmed by melting point determination and also by FT-IR spectral analysis

Drug content

Ten tablets were powdered and the blend equivalent to active dose was weighed and dissolved in suitable quantity of pH 6.8 solution[17,18]. The solution was filtered and analyzed on UV-Spectrophotometer.

List of some marketed products of MDT[47-49]

Trade name	Active drug	Manufacturer
Nimulid : MD	Nimesulide	Panacea Biotech, New Delhi, India
Feldene fast melt	Piroxicam	Pfizer Inc., NY, U.S.A
Zyrof meltab	Rofecoxib	Zydus, Cadila, India
Pepcid RPD	Famotidine	Merck and Co., NJ, U.S.A
Romilast	Montelukast	Ranbaxy Labs Ltd., New Delhi,India
Torrox MT	Rofecoxib	Torrent Pharmaceuticals, Ahmedabad, India
Olanex instab	Olanzapine	Ranbaxy Labs Ltd., New Delhi, India
Zofran ODT	Ondansetron	Glaxo Wellcome, Middlesex, UK
Mosid-MT	Mosapride citrate	Torrent Pharmaceuticals, Ahmedabad, India
Febrectol	Paracetamol	Prographarm, Chateauneuf, France
Maxalt MLT	Rizatriptan	Merck and Co., NJ, U.S.A
Zelapar TM	Selegiline	Amarin Corp., London, UK
Claritin® Redi Tabs®	Loratadine	Scherig corporation
Zyperxa®	Olazepine	Eli Lilly
Resperdal® M-Tab TM	Resperidone	Janssen
Zubrin TM (Pet drug)	Tepoxelin	Scherig corporation
Zelapar TM	Selegiline	Elanl Amarin corporation
Propulsid®	Cisapride	Jannsen

Table 6: Orodispersible products available in Indian market[50]

Trade name	Active drug	Manufacturer
Ugesic	Piroxicam	Mayer organic Ltd.
Torrox MT	Rofecoxib	Torrent phatma
Esulide MD	Nimesulide	Doff Biotech
Vomidon md	Domperidone	Olcare lab
kazoldil MD	Nimesulide	kaizen drugs
Zofer MD	Ondansetron	Sun pharma
Mosid md	Mosapride	Torrent pharma
valus	Valdecoxib	Galen mark
Ondem MD	ondencetrom	Alkem pharma
Nimulid MDT	Nimesulide	Panacea Biotech
Rofixx md	Rofecoxib	Cipla ltd. Mumbai ,India
Olanex Istab	Olanzapine	Ranbaxy Labs Ltd.
Romilast	Montelukast	Ranbaxy Labs Ltd.
Zontec MD	Cetrizine	Zosta pharma India
Nime MD	Nimesulide	Maiden pharma
Lonazep MD	Olnazepine	Sun pharma

Future prospects and research trends in FDTs[51]

There are several biopharmaceutical advantages such as improved efficiency over conventional dosage forms for Mouth dissolving tablets. For example, they require smaller amounts of active ingredient to be effective, improve absorption profiles, and offer better drug bioavailability than regular tablets and capsules. There are still many aspects to improve in the FDT formulations.

Despite advances in the FDT technologies, formulation of hydrophobic drugs is still a challenge, especially when the amount of drug is high. The low dose drugs, such as Loratadine with 10 mg dose, pose little problem, but as the dose increases, the formulation sacrifices its fast disintegrating property. A new technology is being developed to incorporate higher doses of hydrophobic drugs without affecting the fast disintegrating property too severely.

The disintegration times of most FDTs on the market are acceptable—i.e., less than 60 seconds—but certainly there is a room for improvement. Because the disintegration time is related to other formulation variables, a balance has to be maintained between shortening the disintegration time and other tablet properties. The tablet hardness, friability, and stability can be further improved to such a level that multitablet packaging in conventional bottles becomes a norm.

The future of FDTs lies in the development of FDTs with controlled release properties. If one FDT can deliver drugs with short half-lives for 12-24 hours, itwould be a quantum improvement in the FDT technology. The added convenience and compliance of such formulations would be enormous.

The future of FDTs also lies in the development of eff ective taste-masking properties. The use of coating poorly tasting drugs is commonly used, but it increases the total volume of the final formulation.

There may be no magic solution to this, but more eff ective use of existing taste masking technologies is expected to alleviate the problems associated with taste masking.

The safety and efficacy profile of drugs in orodispersible tablet is same like their conventional tablet dosage form. Based on conventional techniques, new techniques are developed like Zydis, Wow Tab, Flashtab technology and many more, which leads to getting a patent and new market strategy for orodispersible tablets. This dosage form are gaining market share day by day and becoming a better choice of acceptance.

In addition, the ability to formulate drugs in large doses will bring another important technological advance. In general, the FDT formulations require large amounts of excipients, and having large doses of drug will only make the final formulation too big to handle. An FDT formulations that would require fewer excipients than the drug itself would be a breakthrough. While the problems to be solved are not easy, the history suggests that it is just a matter of time before they are solved.

CONCLUSION

Recently there is significant amount of non-compliance among the patients and hence there is a need to design the patient-oriented drug delivery systems. Orally disintegrating tablets have better patient acceptance and offer improved biopharmaceutical properties, improved efficacy and better safety as compared with conventional oral dosage forms. Recent trends of patient oriented dosage form to achieve patient compliance.

By using new manufacturing technologies, many drugs can be formulated in the form of mouth dissolving tablets to provide the advantages of liquid medication in the form of solid preparation. FDT need to be formulated for pediatric, geriatric, bedridden, psychotic patients, for those patients who are busy in traveling, patients who are may not have access to water.

The key to FDT formulations is fast disintegration, dissolution, or melting in the mouth, and this can be achieved by producing the porous structure of the tablet matrix or adding superdisintegrant and/or eff ervescent excipients. The clinical studies show FDTs can improve patient compliance, provide a rapid onset time of action, and increase bioavailability.

Considering the many benefits of FDTs, it is only a matter of time until a majority of oral formulations are prepared in FDT forms.

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