International Standard Serial Number (ISSN): 2249-6807

International Journal of Institutional Pharmacy and Life Sciences 6(1): January-February 2016

INTERNATIONAL JOURNAL OF INSTITUTIONAL PHARMACY AND LIFE SCIENCES

Pharmaceutical Sciences

Review Article……!!!

Received: 06-01-2016; Revised: 08-02-2016; Accepted: 09-02-2016

A REVIEW ON : MOUTH DISSOLVING TABLETS

V. S. Aher*[1], B.A. Bhairav[1], R. B. Saudagar[2]

1.Department of Quality Assurance Technique, R.G.Sapkal College of Pharmacy Anjaneri, Nasik, 422003

2.Department of Pharmaceutical Chemistry, R.G.Sapkal College of Pharmacy Anjaneri, Nasik, 422003

Keywords:

Mouth dissolving tablet, Conventional techniques, Rapid Disintegration

For Correspondence:

V. S. Aher

Department of Quality Assurance Technique, R.G.Sapkal College of Pharmacy Anjaneri, Nasik, 422003

E-mail:

vaishaliaher91@gmail.com

ABSTRACT

Mouth dissolving tablets are solid dosage forms containing drugs that disintegrate in the oral cavity within less than one minute leaving an easy to swallow residue. In the recent trend the development of mouth dissolving tablets formulation is emerging and gaining popularity because it is easy to administer and leads to better patient compliance. These dosage forms are placed in the mouth, allowed to disperse or dissolve in the saliva. The release the drug as soon as they come in contact with the saliva, thus obviating the need for water during administration. The aim of this article is to review the progress of the evolving technologies and super disintegrating agents in the formulation, manufacturing and evaluation of these tablets. This article also discusses the new evaluation methodologies for these orally disintegrating tablets. Various modifications in the conventional evaluation and use of specialized instruments are found to be essential in the testing of these dosage forms. In the present review the formulation techniques and different technologies are discussed.

INTRODUCTION

Drug delivery systems became sophisticated as pharmaceutical scientists acquire a better understanding of the physicochemical and biochemical parameters pertinent to their performance. Over the past three decades, mouth dissolving or orally disintegrating tablets have gained considerable attention as a preferred alternative to conventional tablets due to better patient compliance. Polymer coating enables the formulation of mouth dissolving and taste masking of bitter taste drugs-thereby giving better patient compliance [4]. Tablets that are fast disintegrate or dissolve rapidly in the patient's mouth, are convenient for young children, aged and patients with swallowing difficulties [5]. For these formulations, the small volume of saliva is usually sufficient to result in tablet disintegration in the oral cavity [6]. The medication then be absorbed partially or entirely into the systemic circulation from blood vessels in the sublingual mucosa, or it can be swallowed as a solution to be absorbed from the gastrointestinal tract (GIT) [7]. The bioavailability of some drugs may be enhancing due to absorption of drugs in oral cavity and also due to pregastric absorption of saliva containing dispersed drugs that pass down into the stomach. The amount of drug that is subject to first pass metabolism is reduced as compared to mouth dissolving tablets [8]. Orally disintegrating tablets contain wide variety of pharmaceutical active ingredients covering many therapeutic categories. The time for disintegration of orally disintegrating tablets are generally considered less than one minute. Orally disintegrating tablets are characterized by high porosity, low density and low hardness. When administered, an in-situ suspension is created in the oral cavity as the tablet disintegrates and is subsequently swallowed [9]. Drug delivery systems became sophisticated as pharmaceutical scientists acquire a better understanding of the physicochemical and biochemical parameters pertinent to their performance. A Mouth dissolving drug delivery system, in most cases, is a tablet that dissolves or disintegrates in the oral cavity without the need of water or chewing. These are also called melt-in-mouth tablets, rapimelts, spongy tablets, oro-dispersible, quick dissolving or rapid disintegrating tablets. Direct compression one of the techniques requires the incorporation of a super disintegrant into the formulation the use or highly water soluble excipients to achieves fast tablet disintegration. In Pharmacopoeia (EP), which defines oro –dispersible tablets as "uncoated tablets indented to be placed in the mouth where they disperse rapidly before being swallowed". European pharmacopoeia also specifies that the oro-dispersible tablets should disintegrate within 3 minutes when subjected to conventional disintegration test

used for tablets and capsules. According to European Pharmacopoeia another definition is "Rapid disintegration tablet is solid unit dosage form that is placed in the mouth, allowed to disperse/dissolve in the saliva and then swallowed without need of water". One important drawback of solid dosage forms is the difficulty in swallowing (dysphasia) or chewing in some patients particularly pediatric and geriatric patients. Approximately one third of the population (mainly pediatric and geriatric) has swallowing difficulties, resulting in poor compliance with oral tablet drug therapy, which leads to reduced overall therapy effectiveness. For this reason, tablets that can rapidly dissolve or disintegrate in the oral cavity have attracted a great deal of attention. The fast dissolving solid dosage form turns into a soft paste for swallowing, and thus it is free of risk of chocking.[10-21]

Mouth dissolving tablet

This is an innovative tablet technology where the dosage form containing active pharmaceutical ingredients disintegrates rapidly, usually in a matter of seconds, without the need for water, providing optimal convenience to the patient. The European Pharmacopoeia defines MDTs as a tablet that can be placed in the mouth where it disperses rapidly before swallowing. Researchers have formulated MDT for various categories of drugs, which are used for therapy in which rapid peak plasma concentration is required to achieve desired pharmacological response. These include neuroleptics, cardiovascular agents, analgesics, anti-allergic and drugs for erectile dysfunction.

Significance of MDTs: [22, 23]

MDTs offer dual advantages of solid dosage forms and liquid dosage forms along with special Features which include:

- Accurate dosing: Being unit solid dosage forms, provide luxury of accurate dosing, easy portability and manufacturing, good physical and chemical stability and an ideal alternative for pediatric and geriatric patients.
- Enhanced bioavailability: Bioavailability of drugs is enhanced due to absorption from mouth, pharynx and esophagus.
- Rapid action: Fast onset of therapeutic action as tablet gets disintegrated rapidly along with quick dissolution and absorption in oral cavity.
- Patient compliance: No need of water to swallow the dosage form. Hence, it is convenient for patients who are traveling and do not have immediate access to water.
- Ease of administration: Convenient to administer specially for geriatric, pediatric, mentally disabled and bed ridden patients who have difficulty in swallowing.

- Obstruction free: No risk of suffocation in airways due to physical obstruction when swallowed, thus providing improved safety and compliance.
- Enhanced palatability: Good mouth feels, especially for pediatric patients as taste masking technique is used to avoid the bitter taste of drug.
- Simple packaging: No specific packaging required. It can be packaged in push through blisters.
- Cost effective: Conventional processing and packaging equipments allow the manufacturing of tablets at low cost.

Desired Criteria for MDDS Mouth Dissolving Tablets: [1, 2]

Desired Criteria for MDDS Mouth Dissolving Tablets should:

- Not require water to swallow, but it should dissolve or disintegrate in the mouth in matter of seconds.
- Be compatible with taste masking.
- Be portable without fragility concern.
- Have a pleasing mouth feel.
- Leave minimal or no residue in the mouth after oral administration.
- Exhibits low sensitivity to environmental conditions as humidity and temperature.
- Allow the manufacture of tablet using conventional processing and packaging equipment at low cost.

Salient Features of Mouth Dissolving Drug Delivery System:

- Ease of administration to pediatric, geriatric and psychiatric patients who refuse to swallow tablets.
- To swallow the dosage form, water not required which is highly convenient feature for patients who are depressed.
- Rapid dissolution and absorption of drug, which may produce rapid onset of action.
- Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach, which enhances bioavailability of drugs.

Advantages of Mouth Dissolving Tablets:

- Leave minimal or no residue in mouth after administration.
- Rapid drug therapy intervention.
- Good mouth feel property helps to change the perception of medication as bitter pill particularly in pediatric patients.

- Administration to such as pediatric, geriatric & psychiatric patients.
- Achieve increased bioavailability/rapid absorption through pregastric absorption.
- Convenient for administration and patient compliant for disabled, bedridden patients and for travelers and busy people, who do not always have access to water.
- The risk of chocking or suffocation during oral administration of conventional formulations due to physical obstruction is avoided, thus providing improved safety.
- Beneficial in cases such as motion sickness, suede episodes of allergic attack or coughing, where an ultra rapid onset of action required. An increased bioavailability, particularly in cases of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution of these tablets.
- It provides advantage of solid dosage form in terms of stability and liquid dosage form in terms of bioavailability.
- High degree of vascularization, minimal enzymatic pool and passing of first pass metabolism increase bioavailability of drugs ideally suited for delivering drugs that are absorbed buccally.
- In condition of pain their rapid disintegration also impose a placebo effect before the medicine's effect actually begins and patient get relief quickly.

Limitations of Mouth Dissolving Tablets

- 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.
- Drugs with relatively larger doses are difficult to formulate into MDT.

Drug candidates suitable for Mouth dissolving tablets [3]

Selection of drug candidate for MDT is a very crucial step while developing such dosage forms because of the following factors:

- Drugs which require controlled or sustained release are unsuitable candidates of fast dissolving oral dosage forms.
- Drugs which are very bitter or otherwise unacceptable taste because taste masking cannot be achieved.
- Drugs with a short half-life and frequent dosing.
- Patients who concurrently take anti-cholinergic medications may not be the best candidates for these drugs.

Conventional Technologies used for manufacturing of MDTs:

In the recent past, several new advanced technologies have been introduced for the manufacturing of MDTs with ideal properties like less disintegration time, pleasant mouth feel, exceptional taste masking and sugar free tablets for diabetic patients. The technologies used for manufacturing of MDTs broadly classified in two category one is patented another one is non-patented technologies.

1. Lyophilization or Freeze-drying: [25]

Formation of porous product in freeze-drying process is exploited in formulating MDTs. 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 lightweight 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.

2. Molding: [26]

In this method, molded tablets are prepared by using water-soluble ingredients so that the tablets dissolve completely and rapidly. The powder blend is moistened with a hydroalcoholic solvent and is molded into tablets under pressure lower than that used in conventional tablet compression. The solvent is then removed by air-drying .Molded tablets are very less compact than compressed tablets. These posses porous structure that increase dissolution.

3. Cotton candy process: [47]

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 re-crystallized to have improved flow properties and compressibility. This candy floss matrix is then milled and blended with active ingredients and excipients and subsequently compressed to MDTs.

4. Spray drying: [27, 28, 29, 30]

This technology produces highly porous and fine powders as the processing solvent is evaporated during the process. In this method to prepare MDTs hydrolyzed and non-hydrolyzed gelatin were used as supporting matrix, mannitol as bulking agent and sodium

starch glycolate or crosscarmellose sodium as Superdisintigrant. Disintegration and dissolution were further increased by adding acidic substances like citric acid or alkali substance like sodium bicarbonate. This formulation technique gives porous powder and disintegration time < 20 sec.

5. 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.

6. Melt granulation: [26, 31]

In this process, MDTs can be prepared by incorporating a hydrophilic waxy binder (super polystate) PEG-6-stearate. Super polystate is a waxy material with an m. pt. of 3337°C and a hydrophilic- lipophilic balance of. It not only acts as a binder and increases the physical resistance of tablets, but also helps in the disintegration of tablets as it melts in the mouth and solubilizes rapidly leaving no residue. Super polystate was incorporated in formulation of MDTs by melt granulation method where granules formed by molten form of this material.

7. Phase transition process: [39]

Investigated processes for the disintegration of MDTs by phase transition of sugar alcohols using erythritol (Melting point: 122°C), xylitol (m. pt. 93-95°C), trehalose (97°C), and mannitol (166°C). Tablets were produced by compressing a powder containing two sugar alcohols with high and low melting points and subsequent heating at a temperature between their melting points. Before heating process, the tablets do not have sufficient hardness because of low compatibility. The tablet hardness was increased after heating process, due to the increase of inter particle bonds or the bonding surface area in tablets induced by phase transition of lower melting point sugar alcohol.

8. Sublimation: [32]

The presence of a highly porous structure in the tablet matrix is the key factor for rapid disintegration of MDTs. 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 tabletting process, which sublimated from the formed tablet. Developed MDTs 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°C for 30 min after preparation of tablets.

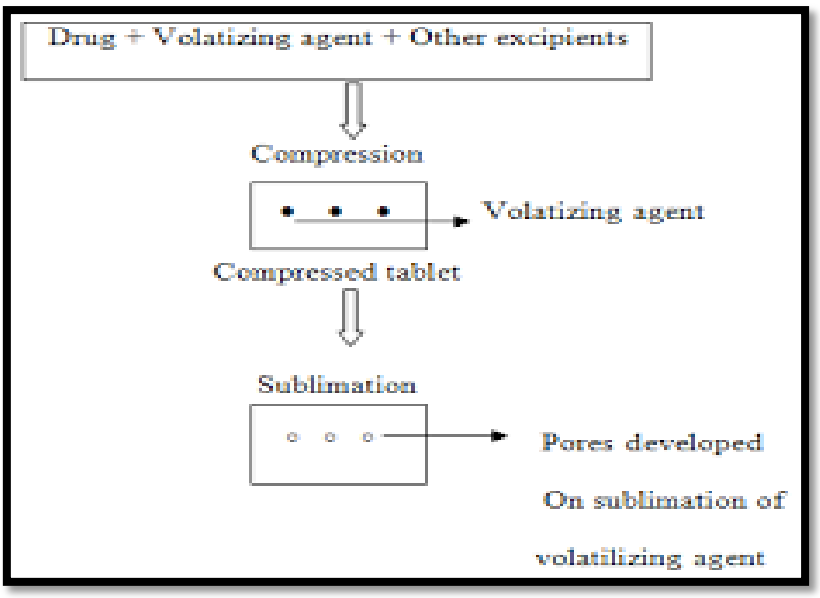

Fig 1: Mechanism of action of sublimation

Table No.1: Relationship between % compressibility and flow ability

No.	% Compressibility	Flow ability
1	5 – 12	Excellent
2	12 – 16	Good
3	18 – 21	Fair Passable
4	23 – 35	Poor
5	33 – 38	Very Poor
6	< 40	Very Very Poor

Table No.2: Angle of Repose as an Indication of Powder Flow Properties

No.	Angle of Repose (°)	Type of Flow
1	< 20	Excellent
2	20 – 30	Good
3	30 – 34	Passable
4	> 34	Very Poor

Table No.3: Weight Variation Specification as per IP

No.	Average Weight of Tablet	% Deviation
1	80 mg or less	±10
2	More than 80 mg but less than 250 mg	±7.5
3	250 mg or more	±5

9. Direct compression methods: [33, 34, 35, 45, 46]

This technique is easy way to formulate MDTs since limited number of processing steps, low manufacturing cost and also accommodate high dose the final weight of tablet can easily exceed that of other production method. The disintegration and dissolution of directly

compressed tablets depends on single or combined effect of disintegrant, water soluble excipients and effervescing agents. Disintegrant efficacy is strongly affected by tablet size and hardness. Disintegration properties can be optimized by medium or low tablet size, low hardness and low physical resistance .It is essential to choose a suitable and an optimum concentration of disintegrant to ensure fast disintegration and high dissolution rates. The addition of water soluble excipients or effervescent agent can further increase dissolution or disintegration properties. Super disintegrants provide fast disintegration due to combine effect of swelling and water absorption. As an effect of swelling of super disintegrant the wetted surface of the carrier increase, which promotes wettability and dispersibility of the system and thereby increase the disintegration and dissolution.

10. Nanonization

A recently developed technology, involves reduction in the particle size of drug to nano size by wet-milling technique. Surface adsorption of the nanocrystals of the drug is done on selected stabilizers for stabilizing them against agglomeration, which are then incorporated into MDTs.

Ingredients used in preparation of MDTs

Ingredients used in MDT formulation are help in quick release of the drug, resulting in faster dissolution.

I. Superdisintigrant [9-12, 8, 14, 15_17]

The most important ingredients of a mouth dissolving tablets are Super disintegrants, which play a major role in the disintegration and dissolution of MDT. Sodium starch glycolate, Ac-di-sol (Crosscarmellose sodium), Crospovidone, Microcrystalline cellulose, Pregelatinised starch are some of the examples of disintegrants. Most of the MDTs consists certain super disintegrants and taste masking agents. It is necessary to select a suitable disintegrant, in an optimum concentration (selected according to critical concentration of disintegrant) to ensure quick disintegration and high dissolution rates. Although superdisintegrants primarily affect the rate of disintegration, high levels, they can also affect mouth feel, tablet hardness and friability. Super disintegrants provide quick disintegration due to combined effect of swelling and water absorption by the formulation. Due to swelling of superdisintegrants, the wetted surface of the carrier increases which promotes the wettability and dispersibility of the system, thus enhancing the disintegration and dissolution.

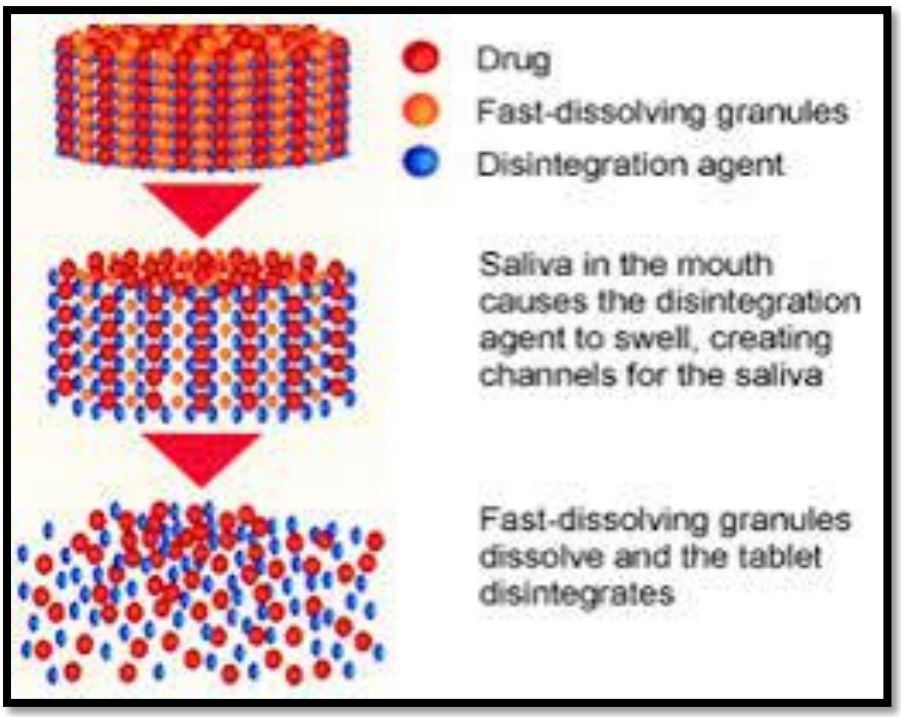

Fig 1: Mechanism of disintegration of mouth dissolving tablet

Role of super-disintegrants in mouth dissolving tablets: [42, 43, 44]

It is essential to choose a suitable disintegrant, in an optimum concentration so as to ensure quick disintegration and high dissolution rates. Disintegrants are agents added to tablet and some encapsulated formulations to promote the breakup of the tablet and capsule "slugs' into smaller fragments in an aqueous environment there by increasing the available surface area and promoting a more rapid release of th They promote moisture penetration and dispersion of the tablet matrix. The disintegrants have the major function to oppose the efficiency of the tablet binder and the physical forces that act under compression to form the tablet. The stronger the binder, the more effective must be the disintegrating agents in order for the tablet to release its medication. Ideally, it should cause the tablet to disrupt, not only into the granules from which it was compressed, but also into powder particles from which the granulation was prepared. Disintegrants are an essential component to tablet formulations. The ability to interact strongly with water is essential to disintegrate function. Combinations of swelling and/or wicking and/or deformation are of disintegrate action. A disintegrate used in granulated formulation processes can be more effective if used both "intragranularly" and "extra-granularly" thereby acting to break the tablet up into granules and having the granules further disintegrate to release the drug substance into solution. However, the portion of disintegrate added intragranularly (in wet granulation processes) is usually not as effective.

Mode of addition [45, 46]

There are three methods of incorporating disintegrating into the tablet:

- Internal addition (Intragranular)
- External addition (Extragranular)
- Partly internal and external.

Mechanism of tablet disintegration [48]

There are four major mechanisms for tablets disintegration as follow:

Swelling

The most widely accepted general mechanism of action for tablet disintegration is swelling. 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 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.

Porosity and capillary action (Wicking)

Disintegration by capillary action is always the first step. 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. Water uptake hydrophilicity of the drug For these types of disintegrants maintenance of porous structure and low interfacial tension towards aqueous fluid is necessary which helps in disintegration.

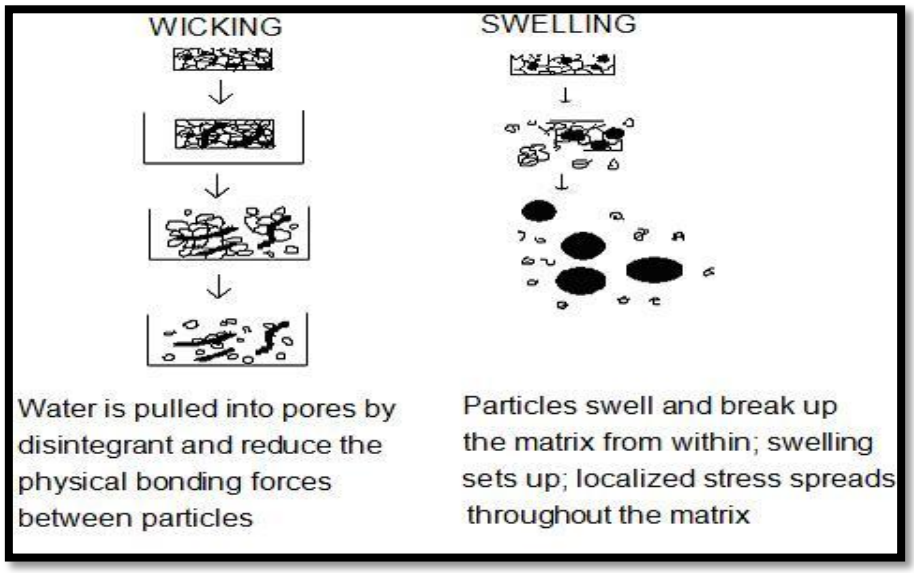

Fig: Mechanism of Superdisintigrant: Porosity and capillary action (Wicking)

Due to disintegrating particle / particle repulsive forces

This mechanism of disintegration attempts to explain the swelling of tablet made with 'non-swellable' disintegrants. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it.

Due to disintegrating particle / particle repulsive forces

Another mechanism of disintegration attempts to explain the swelling of tablet made with non-swellable disintegrants. Guyot Hermann has proposed a particle repulsion theory based on the observation that non-swelling 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.

Due to deformation

During tablet compression, disintegrated 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 extensively deformed during compression. This increase in size of the deformed particles produces a breakup of the tablets.

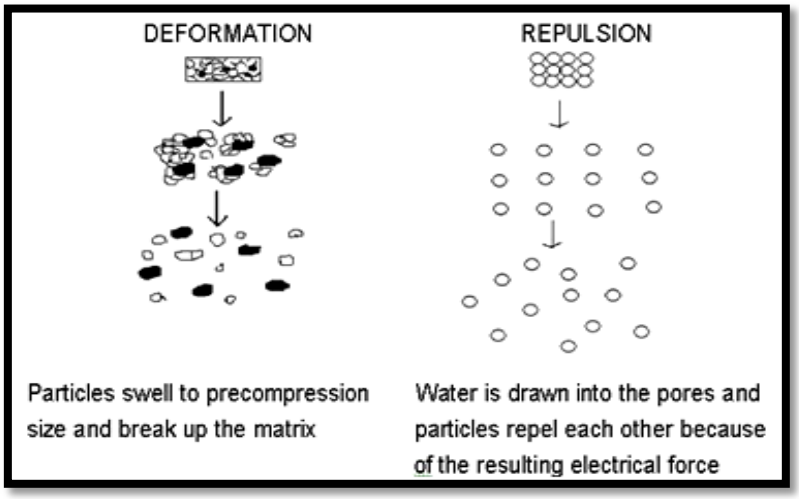

Fig.: Steps involved in repulsion & deformation

Factors affecting action of disintegrants [51, 52]

1. Percentage of disintegrate present in the tablets
2. Type of excipients present in the tablets
3. Combination of disintegrants
4. Presence of surfactant
5. Hardness of tablet
6. Nature of drug substance

Table 4: Some examples of enzymes as a disintegrating agent

No.	Enzyme	Binder
1	Amylase	Starch
2	Starch	Gelatin
3	Cellulose	Cellulose & its derivative

Types of Superdisintigrant

I. Natural

II. Synthetic

III. Co-processed

- **Natural**

These are various plant based material. Plant based material serve as an alternative to synthetic products because of following reasons:

• Local accessibility

• Eco-friendly

• Bio-acceptable

• Renewable source and low price as compared to synthetic products

• Example: Lepidus sativum , Locust bean gum, Isapghula Husk (Plantago ovata), Hibiscus rosa sinesis linn. Mucilage etc.

- **Synthetic**

Advantages of synthetic Superdisintigrant:

• Effective in lower concentrations than starch.

• Less effect on compressibility and flow ability.

• More effective intragranularly

II. Flavours

Flavours and taste-masking agents make the products more palatable and pleasing for patients. The addition of these ingredients assists in overcoming bitterness and undesirable tastes of some active ingredients. For example, example Peppermint flavor , cooling flavor, flavor oils and flavoring aromatic oil, peppermint oil, clove oil, bay oil, anise oil, etc. Aspartame, Sugars derivatives are used as sweeteners.

III. Fillers

Selection of filler also had an important role in deciding the disintegration time. Some examples of fillers are directly compressible spray dried Mannitol, Sorbitol, xylitol, calcium carbonate, magnesium carbonate, calcium.

IV. Surface active agents

The presence of esterase or bile salts (sodium doecyl sulfate, sodium lauryl sulfate, polyoxy ethylene sorbitan fatty acid esters) like surface active agents plays a role in drug release.

V. Lubricants

Lubricants, though not essential excipients, can further assist in making these tablets more palatable after they disintegrate in the mouth. Lubricants remove grittiness and assist in the drug transport mechanism from the mouth down into the stomach. Some examples are Stearic acid, Magnesium stearate, Zinc state, calcium state, talc, polyethylene.

VI. Binder

Binders are added to tablet to add cohesiveness to powders, thus providing the necessary bonding to form granules, which under compaction form a cohesive mass or a compact which is referred to as a tablet. Polyvinylpyrrolidone, Polyvinyl-alcohol, Hydroxypropylmethylcellulose.

VII. Color

Sunset yellow, Amaranth, etc.

Patented Technologies for Fast Dissolving Tablets:

1. Zydis Technology:

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 while 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.

2. Durasolv Technology:

Durasolv is the patented technology of CIMA labs. The tablets made by this technology consist of drug, filler and a lubricant. Tablets are prepared by using conventional tabletting equipment and have good rigidity. These can be packaged into conventional packaging system like blisters. Durasolv is an appropriate technology for product requiring low amounts of active ingredients.

3. Orasolv Technology:

CIMA labs have developed Orasolv Technology. In this system active medicament is taste masked. It also contains effervescent disintegrating agent. Tablets are made by direct compression technique at low compression force in order to minimize oral dissolution time. Conventional blenders and tablet machine is used to produce the tablets. The tablets produced are soft and friable.

4. Flash Dose Technology:

Flash dose technology has been patented by fuisz. Nurofen meltlet, a new form of ibuprofen as melt in mouth tablets prepared using flash dose technology is the first commercial product launched by Biovail Corporation. Flash dose tablets consist of self binding shear form matrix termed as "floss". Shear form matrices are prepared by flash heat processing.

5. Wow tab Technology:

Wow tab technology is patented by Yamanouchi Pharmaceutical Co., WOW means "Without Water". In this process, combination of low mouldability saccharides and high mouldability saccharides is used to obtain a rapidly melting strong tablet. The active ingredient is mixed with a low mouldability saccharide (e.g. lactose, glucose, and mannitol) and granulated with a high mouldability saccharide (e.g. Maltose, oligosaccharides) and compressed into table.

6. Flash tab technology [28, 30]

Ethypharm, Saint Cloud, France has patented the Flash tab technology. Tablets formulated by this technology consist of an active ingredient in the form of micro crystals. Drug micro granules may be prepared by using the conventional techniques like co-acervation, micro encapsulation, and extrusion spheronisation. Reticulated polyvinyl pyrrolidine or carboxy methylcellulose is used as disintegrating agents and carboxy methylcellulose, starch, modified starch, microcrystalline cellulose, carboxy methylated starches, etc are used as Swelling agents. All the processing utilized the conventional tabletting technology, and the tablets produced have good mechanical strength and disintegration time less than one minute. All the processing utilized conventional tabletting technology.

7. Oraquick technology [13,31, 50]

The Oraquick fast-dissolving/disintegrating tablet formulation is patented by K.V Pharmaceuticals. It utilizes taste masking microsphere technology called as micro-masking which does not utilize solvents of any kind, which provides superior mouth feel, significant mechanical strength, and quick disintegration/dissolution of product, therefore, leads to faster and more efficient production. Lower heat of production than alternative fast-dissolving technologies make Oraquick appropriate for heat-sensitive drugs.

8. Zip-lets technology [43]

This technology is patented by passano con Barnago, Italy. It utilizes water-insoluble ingredient combined with one or more effective disintegrants. AdvaTab tablets disintegrate rapidly in less than 30 seconds. These tablets are prepared using polymer coated drug particles that are uniformly dispersed in an ultra-fine, low-water content, rapidly disintegrating matrix with superior organoleptic properties. AdvaTab tablets are compressed using a proprietary, patented, external lubrication system in which the lubricant is applied only to the tablet surface, resulting in robust tablets that are hard and less friable and can be packaged in bottles or blister.

9. Lyoctechnology [44]

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.

10. Pharmaburst technology

Pharmaburst technology is patents by SPI Pharma, New Castle. It utilizes the co-processed 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 the sufficient strength, so they can be packed in blister packs and bottles.

11. Nanocrystal technology

Nanocrystal technology is patented by Elan, King of Prussia. Nanocrystal Technology which includes Lyophilization of colloidal

EVALUATION OF MOUTH DISSOLVING TABLET:

MDTs formulations have to be evaluated for the following evaluation test. [53, 54]

I. 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 were taken and their thickness was recorded using micrometer.

II. Uniformity of weight:

I.P. procedure for uniformity of weight was followed, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of determining the drug content uniformity.

III. Tablet 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 was determined using Monsanto Hardness tester.

IV. Friability:

It is measured of mechanical strength of tablets. Roche friabilator was used to determine the friability by following procedure. A pre weighed tablet was placed in the friabilator. Friabilator consist of a plastic-chamber that revolves at 25 rpm, dropping those tablets at a distance of 6 inches with each revolution. The tablets were rotated in the friabilator for at least 4 minutes. At the end of test tablets were dusted and reweighed, the loss in the weight of tablet is the measure of friability and is expressed in percentage as;

% Friability = loss in weight / Initial weight x 100

V. In-Vivo Disintegration test:

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.

VI. Wetting time:

The method reported by Yunixia et al., was followed to measure tablet wetting time. A piece of tissue paper (12 cm X 10.75 cm) folded twice was placed in a small petridish (ID = 6.5 cm) containing 6 ml of Sorenson's buffer pH 6.8. A tablet was put on the paper, and the time for complete wetting was measured. Three trials for each batch and the standard deviation were also determined.

VII. In vitro dispersion time:

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

REFERENCES

1. Hirani Jaysukh J, Rathod Dhaval A, Vadalia Kantilal R.Orally Disintegrating Tablets: A Review. Tropical Journal of Pharmaceutical Research. 2009 April; 8(2):161-172.
2. Bhowmik Debjit, Chiranjib.B, Krishnakanth, Pankaj, R.Margret Chandira. Fast Dissolving Tablet: An Overview. Journal of Chemical And Pharmaceutical Research 2009; 1 (1):163-177.
3. Udaykumar.M, A.B.N.Nageswarao, T.V.S Vinay Kumar, Giri Veda.V.Fast dissolving Tablets: New-fangled Drug Delivery System A Comprehensive Review. International Journal of Research in Drug Delivery. 2012; 2(3):15-25.
4. Birudaraj R, Berner B, Shen S, Li X. Buccal permeation of buspirone: mechanistic studies on transport pathways. J Pharm Sci. 2005;94:70-78
5. Ishikawa T, Koizumi N, Mukai B. Pharmacokinetics of acetaminophen from rapidly disintegrating compressed tablet prepared using microcrystalline cellulose (PH-M-06) and spherical sugar granules. Chem. Pharm Bull (Tokyo). 2001;49:230232.
6. Price T.M., Blauer K.L., Hansen M., Stanczyk F., L obo R., Bates G.W. Single-dose pharmacokinetics of sublingual versus oral administration of micronized17-beta-estradiol. Obstet Gynecol. 1997; 89:340-345
7. Habib,W., Khankari, R., Hontz, J. Fast-dissolving drug delivery systems, critical review in therapeutics, Drug Carrier Systems, 2000;17:61-72.
8. Chang, R., Guo, X., Burnside, B. A., Couch, R. Fast-dissolving tablets, Pharm. Tech., 2000; 24:5258.
9. Dobetti, L. Fast-Melting Tablets: Developments and Technologies, Pharm. Tech., (Suppl.), 2001; 44-50
10. Lachman, L., Libermann, HA., Schwartz, JB. Pharmaceutical dosage forms: Tablets; 2nd Ed.; USA; 1989; 367-414.
11. Lachman, L., Libermann, HA. The theory and practice of industrial pharmacy; 3rd Ed.; published by Lea and Febiger Varghese; 2003; 1 :346-372.
12. Remington. The science and practice of pharmacy; 21st Ed.; published by Wolters Kuwar (India) pvt Ltd.; New Delhi; 2005; 2: 903-914.
13. Aulton, ME. Pharmaceutics: the science of dosage form design; 2nd Ed.; Churchill Livingstone; USA; 2007; 408-412.
14. Ansel, HC., Allen, LV., Popovich, NG. Ansel's pharmaceutical dosage forms and drug delivery system; 8th Ed.; published by Wolters Kuwar (India) pvt Ltd.; New Delhi; 2005; 260-263.
15. Augsburger, LL., Hoga, SW. Pharmaceutical dosage forms: Tablet; informa Healthcare; 3rd Ed.; vol.;Vol. 2: Rational Designed and Formulation: 217-269,293-313.
16. Ratnaparkhi, MP. Et al. Review on: Fast dissolving tablet; Journal of pharmacy Research; January 2009; 2(1): 5-12.
17. Kandikonda, S. et al. Fast dissolving tablets: an update; International Research Journal of Pharmacy; june 2011; 2(6): 45-53.
18. Sharma, S. et al. Fast dissolving drug delivery system- A review; International Research Journal of Pharmacy; 2011; 2(11): 21-29.
19. Varatharajan, P. et al. Formulation and evaluation of voglibose mouth dissolving tablets by direct compression method; Journal of Pharmacy Research; 2012; 5(2): 749-753.
20. Singh, AK. Et al. Development and evaluation of fast disintegrating tablets of salbutamol sulphate by superdisintegrating agents; International Journal of Pharmaceutical Sciences and Research; 2010; 1(7): 46-53.
21. Raghavendra Rao, NG. et al. Comparison of different suprdisintegrants in designing of fast dissolving tablet of metarolol tartrate; International Journal of Pharmaceutical Sciences and Research; 2010; 1 (4):56-66
22. D. Shukla et al., Mouth Dissolving Tablets I: An Overview of Formulation Technology, Scientia Pharmceutica. 2009; 76; 309– 326.
23. Hirani et al., Orally Disintegrating Tablets: A Review, Tropical Journal of Pharmaceutical Research, April 2009; 8 (2): 163
24. Makino T, Yamada M, and Kikuta J. Fast dissolving tablet and its production.

25. Habib W, Khankari RK, Hontz J. Fast-dissolve drug delivery systems. Crit Rev Ther Drug Carrier Sys 2000; 17:61-72.
26. Van Scoik KG. Solid Pharmaceutical dosage in tablet triturates form and method of producing the same. US Patent 5,082, 667.
27. Allen LV, Wang B. Process for making a particulate support matrix for making a rapidly dissolving dosage form. US Patent 6,207,199; 2001.
28. Allen LV, Wang B. Process for making a particulate support matrix for making a rapidly dissolving tablet. US Patent 5,587,180; 1996.
29. Allen LV, Wang B, Davis LD. Rapidly dissolving tablet. US Patent 5,807,576; 1998.
30. Bhaskaran S, Narmada GV. Rapid Dissolving tablet A Novel dosage form Indian Pharmacist 2002; 1:9-12.
31. Abdelbary G, Prinderre P, Eouani C, Joachim J, Reynier JP, Piccerelle P. The preparation of orally disintegrating tablets using a hydrophilic waxy binder. Int J Pharm 2004; 278:423-33.
32. Koizumi K, Watanabe Y, Morita K, Utoguchi N, Matsumoto M. New method of preparing highporosity rapidly saliva soluble compressed tablets using mannitol with camphor: A subliming material. Int J Pharm 1997; 152:127-31.
33. Rishi RK, The pharma review 2004;2:32
34. Makino T, Yamad M, Kikutaj,et al US Patent1998; 5,939,091.
35. Bolhuis KG, Zuurman, Wrierikte PHG etal Eru.J.Pharm 1997; 5:63.
36. Kintsch KN,Hagen A, Manz E . US Patent1979; 4,134,943.
37. Heinemann Hand Rotte W. US Patent 1976; 3,885,026.
38. Meyers GL, Battist GE, Fuisz RC. Process and apparatus for making rapidly dissolving dosage units and product there form. PCT Patent WC 95/34293A1; 1995.
39. Kuno Y, Kojima M, Ando S, Nakagami H. Evaluation of rapidly disintegrating tablets manufactured by phase transition of sugar alcohols. J Control Release 2005; 105:16-22.
40. Fast Dissolving Tablet- A Review, Online Available at www.thepharmajournal.com
THE PHARMA INNOVATION, ORIGINL ARTICLE, Alok Kumar Gupta*, Anuj Mittal and Prof. K. K. Jha Submitted 2011.09.28. Accepted for publication 2011.12.19. Page no. : 3, 4, 5, 6
41. Gupta VRM, Halakatti PK, Lakshmi Narasu M. Mouth Dissolving Tablets – An Innovative Technology: A Review. Am. J. Pharm Tech Res. 2013; 3(1).
42. P. S. Mohanachandran, P. G. Sindhumol& T. S.Kiran. Superdisintegrants: An Overview. Int. J. of Pharma. Sci. Review and Research. 2011; 6: 105-109.
43. Makino T, Yamada M, Kikuta JI. Fast-dissolving tablet and its production. 1998. US Patent 5,720,974. , Feb 24.
44. T. Kaur, B. Gill, S. Kumar & G. D. Gupta. Mouth Dissolving Tablets: A Novel Approach to Drug Delivery. Int. J. of Curr. Pharm. Res. 2010; 3: 1-7.
45. N. G. R. Rao, T. Ketan& S. Bala. Formulation and evaluation of fast dissolving Tablets of Metoprolol Tartrate using Natural superdisintegrant. Int. J. of Pharm. and Clin. Res. 2010; 2: 40-4
46. G. G. Gajare, S. R. Bakliwal, B. R. Rane, N. A. Gujrathi& S. P. Pawar. Mouth Dissolving Tablet: An Review. Int. J. of Pharm. Res. and Dev. 2011; 6: 280-29.
47. [38]. R. Pahwa& N. Gupta. Superdisintegrants in the Development of Orally Disintegrating Tablets: A Review. Int. J. of Pharm. Sci. and Res. 2011; 2: 2767-2780.
48. Kuno Y, Kojima M, Ando S, Nakagami H. Effect of preparation method on properties of orally disintegrating tablets made by phase transition. Int. J. Pharm. 2008, 355; 87–92.
49. S.B Shirsand, Swamy, D. Nagendra Kumar And M.V Rampure, NoveL COProcessed Superdisintegrants In The Design of Fast Dissolving Tablets, Int. J. of PharmTech Res. , 2010; 2:222-227.
50. Sagar A. Konapure, Prafulla S. Chaudhari, Rajesh J. Oswal, Sandip S. Kshirsagar,Rishikesh V. Antre And Trushal V. Chorage, "Mouth Dissolving Tablets" An Innovative Technology, Int. J. of Curr Pharm. Res. 2011; 2(1):212-220.
51. S.B Shirsand, M.S para, D. Nagendra Kumar And M.V Rampure, NoveL COProcessed Superdisintegrants In The Design Of Fast Dissolving Tablets, Int. J. of PharmTech Res. , 2010; 2:222-227.
52. Sagar A. Konapure, Prafulla S. Chaudhari, Rajesh J. Oswal, Sandip S. Kshirsagar,Rishikesh V. Antre And Trushal V. Chorage, "Mouth Dissolving Tablets" An Innovative Technology, Int. J. of Curr Pharm. Res. 2011; 2(1):212-220.
53. Liebermann HA, Lachman L, Kanig JL. The theory and practice of industrial pharmacy. 3rd ed. USA:Varghese Publishing house; 1990. p. 253-296.
54. Srivastava Saurabh , Bala Rajni, Joshi Baibhav, Rana A.C, Singla Vikas. Mouth dissolving tablet:Afuture compaction. International Research Journal of Pharmacy. 2012;3(8):98-109.