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A REVIEW ON FAST DISSOLVING TABLET

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ABSTRACT

Oral route having the highest patient compliance is regarded as the most convenient, safest and also the most economical method of drug delivery. Fast dissolving tablets (FDT) are one such most advantageous example of the oral drug delivery. These tablets readily dissolve or disintegrate in the saliva i.e. within less than 60 sec without the need for water. They have been formulated for pediatric, geriatric and bedridden patients. Novel FDT technologies address many patient and pharmaceutical needs such as enhanced life cycle management to convenient dosing particularly for pediatric, geriatric and psychiatric patients who have difficulty in swallowing (Dysphasia) conventional tablet and capsules. Such formulations provide an opportunity for product line extension in the many elderly persons will have difficulties in taking conventional oral dosage forms (viz., solutions, suspensions, tablets, and capsules) because of hand tremors and dysphasia. Swallowing problems also are common in young individuals because of their underdeveloped muscular and nervous systems. Other groups that may experience problems using conventional oral dosage forms include the mentally ill, the developmentally disabled, and patients who are uncooperative, on reduced liquid-intake plans, or are nauseated. In some cases such as motion sickness, sudden episodes of allergic attack or coughing, and an unavailability of water, swallowing conventional tablets may be difficult. This review depicts the various aspects of FDT formulation, super-disintegrates and technologies developed for FDT, evaluation tests and marketed formulations in this field.

Key Words: Fast disintegrating tablets, Superdisintegrant, Bioavailability, Patented technology, Evaluation.

INTRODUCTION

Fast dissolving dosage forms can be disintegrated, dissolved, or suspended by saliva in the mouth. This fast dissolving tablet (FDT) disintegrates instantaneously when placed on tongue and releases the drug dissolves or disperses in the saliva. FDTs are useful in patients, like pediatric, geriatric, bedridden, or mentally disabled, who may face difficulty in swallowing conventional tablets or capsules leading to ineffective therapy, with persistent nausea, sudden episodes of allergic attacks, or coughing for those who have an active life style. Fast dissolving tablets are also applicable when local action in the mouth is desirable such as local anesthetic for toothaches, oral ulcers, cold sores, or teething, and to those who cannot swallow intact sustained action tablets/capsules.*[1]* Fast dissolving tablets are also called as Mouth-dissolving tablets, Melt-in mouth tablets, Orodispersible tablets, Rapimelts, Porous tablets, Quick dissolving tablets etc. FDT are those when put on tongue disintegrate instantaneously releasing the drug which dissolve or disperses in the saliva. *[2]* Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases, bioavailability of drug is significantly greater than those observed from conventional tablets dosage form. The advantage of mouth dissolving dosage forms are increasingly being recognized in both, industry and academics. *[3]*

United States Food and Drug Administration (FDA) defined ODT as "A solid dosage form containing medicinal substance or active ingredient which disintegrates rapidly usually within a matter of seconds when placed upon the tongue."*[4]* The disintegration time for ODTs generally ranges from several seconds to about a minute. The significance of these dosage forms is highlighted by the adoption of the term, "Orodispersible Tablet", by the European Pharmacopoeia which describes it as a tablet that can be placed in oral cavity where it disperses rapidly before swallowing. *[5]*

Drug selection criteria *[6]*

The ideal characteristics of a drug for oral dispersible tablet include

- Ability to permeate the oral mucosa
- At least partially non-ionized at the oral cavity pH
- Have the ability to diffuse and partition into the epithelium of the upper GIT
- Small to moderate molecular weight
- Low dose drugs preferably less than 50mg
- Short half life and frequent dosing drugs are unsuitable for ODT
- Drug should have good stability in saliva and water

Advantages of FDT: *[7, 8]*

Administration to the patients who cannot swallow, such as the elderly, stroke victims, bedridden patients, patients affected by renal failure and patients who refuse to swallow such as pediatric, geriatric and psychiatric patients.

- Rapid drug therapy intervention
- Achieve increased bioavailability/rapid absorption through pre-gastric absorption of drugs from mouth, pharynx and esophagus as saliva passes down
- Convenient for administration and patient compliant for disabled, bedridden patients and for travelers and busy people, who do not always have access to water
- Good mouth feel property helps to change the perception of medication as bitter pill particularly in pediatric patients

Disadvantage *[9]*

- Fast dissolving tablet is hygroscopic in nature so must be keep in dry place.
- Some time it possesses mouth feeling
- MDT requires special packaging for properly stabilization & safety of stable product.

Salient Features *[10]*

- Ease of administration to patients who refuse to swallow a tablet, such as pediatric and geriatric patients and, psychiatric patients.
- Convenience of administration and accurate dosing as compared to liquids
- Rapid dissolution of drug and absorption which may produce rapid, onset of action
- Some drugs are absorbed from the pharynx and esophagus as the saliva passes down into the stomach, in such cases bioavailability of drugs is increased.
- Ability to provide advantages of liquid medication in the form of solid preparation
- Pre-gastric absorption can result in improved bioavailability and as a result of reduced dosage, improved clinical performance through a reduction of unwanted effects.

Drug Candidates Suitable For Fast Disintegrating Tablets (FDT) *[11]*

Several factors must be considered while selecting an appropriate drug candidate for development of orally fast disintegrating dosage forms.

- 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.
- Patients with Sjogren‟s syndrome or dryness of the mouth due to decreased

saliva production may not be good candidates for FDT formulations.

- Drugs with a short half-life and frequent dosing.

CONVENTIONAL TECHNOLOGIES FOR FAST DISSOLVING TABLETS:

1. Freeze drying or Lyoplilization ***[****12-16]*

A process, in which water is sublimated from the product after freezing, is called freeze drying. Freeze- dried forms offer more rapid dissolution than other available solid products. The lyophilization processes imparts glossy amorphous structure to the bulking agent and sometimes to the drug, thereby enhancing the dissolution characteristic of the formulation. The entire freeze drying process is done at nonelevated temperature to eliminate adverse thermal effects that may affect drug stability. The major disadvantages of lyophilization technique are that it is expensive and time consuming; fragility makes conventional packaging unsuitable for these products and poor stability under stressed conditions and their limited ability to accommodate adequate concentration of drugs.

2. Direct compression *[17, 18]*

Easiest way to manufacture tablets is direct compression. Low manufacturing cost, conventional equipments and limited number of processing steps led this technique to be a preferable one. However disintegration and dissolution of directly compressed tablets depend on single or combined effect of disintegrate, water soluble excipients and effervescing agents. It is essential to choose a suitable and an optimum concentration of disintegrate to ensure quick disintegration and dissolution. Superdisintegrants are newer substances which are more effective at lower concentrations with greater disintegrating efficiency and mechanical strength. On contact with water the superdisintegrants swell, hydrate, change volume or form and produce a disruptive change in the tablet. Effective superdisintegrants provide improved compressibility, compatibility and have no negative impact on the mechanical strength of formulations containing high dose drugs. The type of disintegrants and its proportion are of prime importance. Also factors to be considered are particle size distribution, contact angle, pore size distribution and water absorption capacity.

3. Molding *[19]*

Molded tablets, usually prepared from soluble ingredients, by compressing a powder mixture which is moistened with a solvent, into mould plates to form a wetted mass. Recently, molded forms have been prepared directly from a molten matrix, in which the drug is dissolved or dispersed or by evaporating the solvent from a drug solution or suspension at a standard pressure. Usually molded tablets are compressed at a lower

pressure than are conventional are conventional tablets, and possess a porous structure that hastens dissolution. To improve the dissolution rate, the powder blend usually has to be passed through a very fine screen. Tablet produced by molding are solid dispersion. Molded tablets disintegrate more rapidly and offer improved taste because the dispersion matrix is in general made from water soluble sugars. The active ingredients in most cases are absorbed through the mucosal lining of the mouth. Unfortunately, moulded tablets typically do not possess great mechanical strength. Erosion and breakage of the moulded tablets often occurs during tablet handling and when blister pockets are opened.

4. Mass extrusion *[20, 21]*

This technology involves softening the active blend using the solvent mixture of water soluble polyethylene glycol, using methanol and expulsion of softened mass through the extruder or syringe to get a cylinder shaped extrude which are finally cut into even segments using heated blade to form tablets. This process can also be used to coat granules of bitter drugs to mask their taste. Mass extrusion was the technique used for preparing taste masked granules. The tablet was prepared with different super disintegrate e.g. sodium starch glycolate, croscarmellose sodium and crosspovidone etc.

5. Melt granulation *[22]*

Melt granulation technique is a process by which pharmaceutical powders are efficiently agglomerated by a meltable binder. The advantage of this technique compared to a conventional granulation is that no water or organic solvents is needed. For accomplishing this process, high shear mixers are utilized, where the product temperature is raised above the melting point of binder by a heating jacket or by the heat of friction generated by impeller blades. This approach to prepare FDT with sufficient mechanical integrity, involves the use of a hydrophilic waxy binder (Superpolystate©, PEG-6-stearate). Superpolystate© is a waxy material with a melting point of 33–37°C and a HLB value of 9. So, it will not only act as a binder and increase the physical resistance of tablets but will also help the disintegration of the tablets as it melts in the mouth and solublises rapidly leaving no residues.

6. Phase transition process *[23]*

Kuno et. al. Investigated processes for the disintegration of MDTs by phase transition of sugar alcohols using erythritol (m. pt. 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.

7. Cotton candy process *[24]*

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 10 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 FDTs.

8. Spray drying *[25, 26]*

This technology produces highly porous and fine powders as the processing solvent is evaporated during the process[29]. In this method to prepare FDTs hydrolyzed and nonhydrolyzed gelatin were used as supporting matrix, mannitol as bulking agent and sodium starch glycolate or crosscarmellose sodium as superdisintegrant. 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.

IMPORTANT PATENTED TECHNOLOGIES FOR FAST DISSOLVING TABLET *[27-31]*

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 material 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.

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 100 is used to produce the tablets. The tablets produced are soft and friable.

Table 1: -Commercially available mouth dissolving tablets

Techniques	Marketed Products	Brand Name	Active Constituent	Company
Freeze Drying/ Sublimation	Zydis	Zubrin	Tepoxalin	Schering Corporation
	Quicksolv	Propulsid quicksolv	Cisapride monohydrate	Janseen Pharmaceutica
	Lyoc	Paralyoc	Acetaminophen	Cephlon
	Nanocrystal	Abbott's Tricor	Fenofibrate	Elan
Effervescent	Orasolv	Tempra Quicklets	Acetaminophen	Bristol-Myers Squibb
Spray Drying	Advatab	Unison	Diphenhydramine Hydrocloride	Eurand
Solid Dispersion	Flash Dose	Zolpidem MDT	Zolpidem Tartrate	Biovail
	Shear Form	Tiazac	Diltizen Hydrochloride	Bioavail
Highly Water Soluble Excipients	Wowtab	Benadryl Fast Melt	Diphenhydramine Citrate	Pfizer

4. **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 (eg. Maltose, oligosaccharides) compressed into tablet.

5. **Flash tab Technology:**

Prographarm laboratories have patented the Flash tab technology. Tablet prepared by this system consists of an active ingredient in the form of micro crystals. Drug micro granules may be prepared by using the

conventional techniques like coacervation, micro encapsulation and extrusion spheronisation. All the processing utilized conventional tabletting technology.

6. OraQuick:

The OraQuick fast dissolving / disintegrating tablet formulation utilize a patented taste masking technology. KV Pharmaceutical claims its microsphere technology, known as MicroMask, has superior mouth feel over taste-masking alternatives.

7. Nanotechnology:

For fast dissolving tablets, Elan's proprietary NanoCrystal technology can enable formulation and improve compound activity and final product characteristics. Decreasing particle size increases the surface area, which leads to an increase in dissolution rate. This can be accomplished predictably and efficiently using NanoCrystal technology. NanoCrystal™ Fast dissolving technology provides Pharmacokinetic benefits of orally administered nanoparticles (<2 microns) in 103 the form of a rapidly disintegrating tablet matrix. Product differentiation based upon a combination of proprietary and patentprotected technology elements.

SUPER DISINTEGRANTS USED IN FDT *[32, 33]*

As day's passes, demand for faster disintegrating formulation is increased. So, pharmacist needs to formulate disintegrants i.e. Superdisintegrants which are effective at low concentration and have greater disintegrating efficiency and they are more effective intragranularly.

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. Various types of Super disintegrants used are as follows –

- Crosspovidone
- Microcrystalline cellulose
- Sodium starch glycollate
- Sodium carboxy methyl cellulose or cross carmelose sodium
- Pregelatinzed starch
- Calcium carboxy methyl cellulose.

EVALUATION OF POWDER PROPERTIES OF TABLET *[34]*

The quality of tablet, once formulated by rule, is generally dictated by the quality of physicochemical properties of blends. There are many formulation and process variables involved in mixing and all these can affect the characteristics-of blends produced.

The various characteristics of blends tested are as given below:

1. Angle of Repose:

The frictional force in a loose powder can be measured by the angle of repose. It is

defined as, the maximum angle possible between the surface of the pile of the powder and the horizontal plane. If more powder is added to the pile, it slides down the sides of the pile until the mutual friction of the particles producing a surface angle ω, is in equilibrium with the gravitational force. The angle of repose was determined by the funnel method suggested by Newman. Angle of repose is determined by the following formula;

$$\tan \omega = h/r$$

$$\text{Therefore, } \omega = \tan^{-1} h/r$$

Where ω = Angle of repose

h = height of the cone

r = Radius of the cone base

Angle of Repose less than 30° shows the free flowing of the material.

2. Bulk Density:

Density is defined as weight per unit volume. Bulk density, Pb , is defined as the mass of the powder divided by the bulk volume and is expressed as gm/cm^3. The bulk density of a powder primarily depends on particle size distribution, 'particle shape and the tendency of particles to adhere together. There are two types of bulk density. The particles are pack in such a way so as to leave large gaps between their surfaces 'resulting up in light powder of low bulk density. Here the smaller particles shift between the large particles resulting in heavy powder of high bulk density. Bulk density is very important in the size of containers needed for handling, shipping, and storage of raw material and blend. It is also important in size blending equipment. A standard procedure used for obtaining bulk density or its reciprocal bulkiness is given, below

A sample of about 50 cm^3 (blend) is carefully introduced in a 100ml graduated cylinder. The cylinder is dropped onto a hard wood surface three times from a height of 1 inch at two second interval. The bulk density is then obtained by dividing the weight of sample in gm by final volume in cm^3.

$$\mathbf{Pb=M/Vp}$$

Where,

Pb = Bulk Density

M = Weight of sample in gm

V = Final volume of blend in cm_3

3. Bulkiness:

Specific bulk volume or reciprocal of bulk density is called bulkiness or bulk. Bulkiness increases with a decrease in particle size. In mixture of material of different sizes, however the smaller particle shifts between the larger particles and tends to reduce the bulkiness. The bulkiness can be calculated by the following formula

$$\mathbf{Bulkiness = 1 / pb}$$

Where, pb = Bulk Density

Loose bulk density it is defined as the ratio of weight of blend in gms to the loose bulk volume (untapped volume) in cm^3 loose bulk density is given by

Loose bulk density (pu) = Weight in gms / Vb

Where, Vb = Bulk volume (untapped volume)

4. Void Volume:

The volume of the spaces is known as the void volume "v" and is given by the formula

v = Vb - Vp

Where, Vb = Bulk volume (volume before tapping) V = True volume (volume after tapping)

5. Porosity:

The porosity (€) of powder is defined as the ratio of void volume to the bulk volume of the packaging. The porosity of the powder is given by

€ = Vb - Vp/ Vp

€ = 1 - Vp/Vb

Porosity is frequently expressed in percentage and is given as,

% € = (1 - Vp/ Vb) x 100

The porosity of powder indicates the types of packaging a powder undergoes when subject to vibrations, when stored, or in tablet machine when passed through hopper or feed frame.

6. Percent Compressibility:

It is an important measure obtained from bulk density and is defined as,

C= (Pb-Pu) / Pb x 100

If the bed of particles is more compressible the blend will be less flowable and flowing materials.

EVALUATION TEST FOR FAST DISSOLVING TABLET *[35, 36]*

Tablets from all the formulation were subjected to following quality control test.

1. General Appearance:

The general appearance of a tablet, its visual identity and over all "elegance" is essential for consumer acceptance. Include 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.

2. Size and Shape:

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

3. 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.

4. 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.

Table 2:- I.P. Specification for uniformity of weight

Sr.No.	Average Weight Of Tablets(Mg)	Maximum Percentage Different Allowed
1.	130 or less	10
2.	130-324	7.5
3.	More than 324	5

5. 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 Monsato Hardness tester.

6. Friability:

It is measured of mechanical strength of tablets. Roche friabilator was used to determine the friability by following procedure. A preweighed 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

7. In Vivo Dsintegration test:

The test was carried out on 6 tablets using the apparatus specified in I.P.-1996 distilled water at 37ºC ± 2ºC was used as a disintegration media and the time in second taken for complete disintegration of the tablet with no palable mass remaining in the apparatus was measured in seconds.

8. 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. 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.

9. Stability Study (Temperature Dependent):

The fast dissolving tablets are packed in suitable packaging and stored under the following conditions for a period as prescribed by ICH guidelines for accelerated studies.

- 40 ± 1°C
- 50 ± 1°C
- 37 ± 1° C and RH 75% ± 5%

The tablets were withdrawn after a period of 15 days and analyzed for physical characterization (Vissual defects, Hardness, Friability, Disintegrations, and Dissolution etc.) and drug content.

CONCLUSION

Orally disintegrating tablets have potential advantages over conventional dosage forms, with improved patient compliance, convenience, bioavailability and rapid onset of action. They are a very good alternative for drug delivery to geriatric and pediatric patients. They have significant advantages of both solid and liquid dosage forms, as they remain solid during storage, which aid in stability of dosage forms and transform into liquid form within few seconds after its administration. As a result of the variety of technologies for its formulation, several commercial products are available in the market. Thus ODT has tremendous scope for being the delivery system for most of the drugs in near future.

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