Review Article

FAST DISSOLVING TABLETS- AN ONGOING TREND IN PHARMACEUTICAL INDUSTRY

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ABSTRACT

Fast dissolving tablets are a novel drug delivery system which provides the fastest onset of action and rapid pharmacological effects. This dosage form can be administered easily under any circumstances without accessing the need of water. These dosage forms are gaining popularity because of it convenient way of administration. FDTs are having more advantageous properties than conventional tablets. Fast dissolving tablets are also more preferable than fast dissolving films as high drug loading can be possible and can be easily handled. Fast dissolving tablets can be formulated by using natural and synthetic superdisintegrants along with other excipients. Formulated FDTs are evaluated for precompression parameters and post compression parameters. Hence, fast dissolving tablets are found as simple, convenient, flexible and versatile dosage form.

Keywords: superdisintegrants, swelling, wicking, versatile, good solubility.

INTRODUCTION

Drug delivery system (DDS) can be defined as an introduction of a therapeutic substance into the body to improve its efficacy and safety and which acts as an interfaces between the patient and the drug. Drug may be administered into the human body by several kind of routes, but oral route has been one of the most popular and used route for both conventional as well as novel drug delivery because of low cost of therapy, pain avoidance, self-medication, ease of ingestion, leading to high levels of patient compliance, and it did not require sterile conditions. However, this form of dosage has also associated with some limitation like motion sickness, sudden episodes of allergic attacks or coughing and unavailability of water, but one important drawback is difficulty in swallowing. To overcome these problems, fast dissolving tablets (FDT) have been developed, which having good hardness, dose uniformity, easy administration and serves as the first preferable choice of dosage form for pediatrics, geriatrics and travelling patients. FDTs are also known as “fast-melting, mouth dissolving, orally dissolving, rapimelts, quick porous, oral disintegrating or disperse”. Fast dissolving tablets can define as "A solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed under the tongue. Fast Dissolving Tablet has a pleasing mouth feel, and it not required water to swallow. FDT easily dissolved or disintegrates in saliva within a few seconds (15 sec to 3 min) without the need of drinking water or chewing, leaves no residue in the mouth when administered and less sensitive to environmental conditions like temperature, humidity. Some FDT tablets are designed to dissolve in saliva remarkably fast, within a few seconds, and are called true fast-dissolving tablets. Superdisintegrants agents are added alone or in combination to enhance the rate of tablet disintegration in the oral cavity and are more appropriately termed as fast-disintegrating tablets, as they may take about one minute to disintegrate completely[1]. Researchers are attracted to this development of this dosage form because of its promising activity of getting rapidly dispersed. Fast dissolving tablets are highly accepted fast growing drug delivery system. According to US FDA orodispersible tablets are defined as “A solid dosage form containing medicinal substances which disintegrates rapidly usually within a matter of seconds, when placed upon the tongue”.

European pharmacopeia defined orodispersible tablet as a “tablet that is to be placed in the mouth where it disperses, rapidly before swallowing despite various terminologies used”. Fast dissolving tablets are the best alternate to deliver the drug having bitter taste and poor bioavailability. The orodispersible tablets dissolves in the oral cavity without drinking water where it disintegrates within a fraction of seconds. The disintegrated mass slides down smoothly along the esophagus with the help of saliva, so even people who have swallowing or chewing difficulties can take it with ease.

Advantages and disadvantages of fast dissolving tablets (FDTs)

Table 1: Advantages and disadvantages of fast dissolving tablets

S. No.	Merits	Demerits
1	Water is not required for the administration of FDTs.	Special packaging is required to prevent moisture absorption.
2	No difficulty in swallowing	Careful handling is needed.
3	Palatable taste.	Hygroscopic conditions may be formed.
4	Easy acceptance by gediatrics, pediatrics, uncooperative and unconscious patients.	
5	More patient compliance.	
6	Ability to offer advantages of liquid medication in the form of solid preparation	
7	Easily accessible by travelling person and mentally disabled individual.	
8	Rapid onset of action.	
9	Provide superior pharmacological effects.	
10	Cost effective.	

KEY FEATURES OF FDTS[2]

- Ease of administration
- Rapid onset of action
- Accurate dosing of drug
- Enhanced bioavailability
- High patient compliance
- Obstruction free and safe
- Good stability
- Simple packaging
- New business opportunities
- More cost effective
- Versatile technology

METHODS USED TO MANUFACTURE FAST DISSOLVING TABLETS

1. **Sublimation**: in this method, a subliming material like camphor is removed by sublimation from compressed tablets and high porosity is achieved due to the formation of many pores where camphor particles previously existed in the compressed tablets. Subliming material is sublimed from the dried granules by vacuum exposure.
2. **Direct compression**: It is the easiest method of all for the formulation of conventional dosage form. Conventional equipment, commonly available excipients and a limited number of processing steps are involved in direct compression technique, i.e. Simple mixing of the ingredients and directly compressing them into tablet form by tablet punching equipment. No need of starch paste and wet granulation. It is a single step process without any tedious method.
3. **Freeze drying**: In this method, the material is frozen to bring it below the eutectic point. It is then dried out to reduce the bound moisture to the required volume.
4. **Spray drying:** in this technique, a suspension is prepared containing hydrolyzed and unhydrolyzed gelatin as a supporting agent for matrix, bulking agent, and disintegrants. This suspension is then spray dried to yield a porous powder which is then compressed into tablets.
5. **Tablet molding**: process is of two types, solvent moulding and heat moulding.
   In **solvent moulding method** the powder blend is moistened with a hydroalcoholic solvent followed by pressing into mold plates to form wetted mass. The solvent is then removed by air drying. In **heat moulding method**, a suspension containing drug, agar, and sugar is prepared; this suspension is then poured into blister packaging wells, followed by solidifying the agar at room temperature to form jelly and drying at 30o c under vacuum.
6. **Mass extrusion**: in this method, the active blend is softened using the solvent mixture of water-soluble polyethylene glycol and methanol. This softened mass is then subjected for subsequent expulsion through the extruder or syringe to get a cylinder of the product into seven segments using heated blade to form tablet. The dried cylinder can be used to coat granules for bitter drugs for achieving bitter taste masking[3].

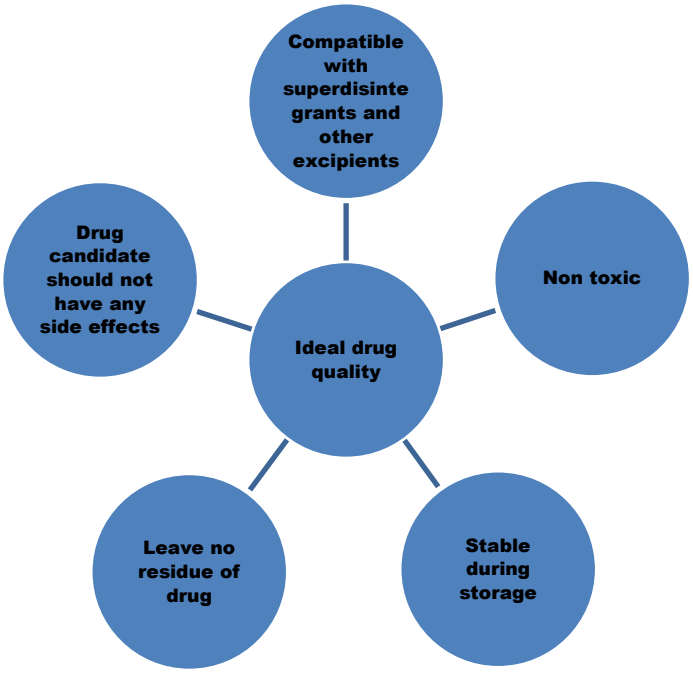

Fig. 1: Ideal drug quality required to incorporate into fast dissolving tablets

SUPERDISINTEGRANTS

Disintegrating agents are substances routinely included in the tablet formulations to aid in the break-up of the compacted mass into the primary particles to facilitate the dissolution or release of the active ingredients when it is put into a fluid environment. They endorse moisture penetration and dispersion of the tablet matrix. The major function of disintegrants is to oppose the efficiency of the tablet binder and physical forces that act under compression to structure the tablet. Recently new materials termed as "superdisintegrants" have been developed to improve the disintegration processes. Superdisintegrants are another version of super-absorbing materials with tailor-made swelling properties. These materials are not planned to absorb significant amounts of water or aqueous fluids, but planned to swell very fast. Superdisintegrants are used as a structural weakener for the disintegrable solid dosage forms. They are physically dispersed within the matrix of the dosage form and will expand when the dosage form is exposed to the wet environment. These newer substances are more effective at lower concentrations with greater disintegrating efficiency and mechanical strength. Superdisintegrants are generally used at a low level in the solid dosage form, typically 1 - 10 % by weight relative to the total weight of the dosage unit. Their particles are generally small and porous, which allow for rapid tablet disintegration in the mouth without an objectionable mouth-feel from either large particles or gelling. The particles are also compressible which improves tablet hardness and its friability. Effective superdisintegrants provide improved compressibility, compatibility and have no negative impact on the mechanical strength of formulations containing high-dose drugs. Generally, one gram of superdisintegrant absorbs 10-40 g of water or aqueous medium. After absorption, swelling pressure and isotropic swelling of the superdisintegrants particles create stress concentrated areas where a gradient of mechanical properties will exist due to which whole structure will break apart.

Superdisintegrant is used as an additive in the tablet formulation; it has to meet certain criteria other than its swelling properties. The requirement placed on the tablet disintegrant should be clearly defined.

The ideal disintegrant should have:

1. Poor solubility.
2. Poor gel formation.
3. Good hydration capacity.
4. Good moulding and flow properties.
5. No tendency to form complexes with the drugs.
6. Good mouth feel.
7. It should also be compatible with the other excipients and have desirable tableting properties.

Mechanism of superdisintegrants

Superdisintegrants are used to improve the efficacy of solid dosage forms. This is achieved by various mechanisms. The mechanism by which the tablets are broken into small pieces and then produces a homogeneous suspension is based on:

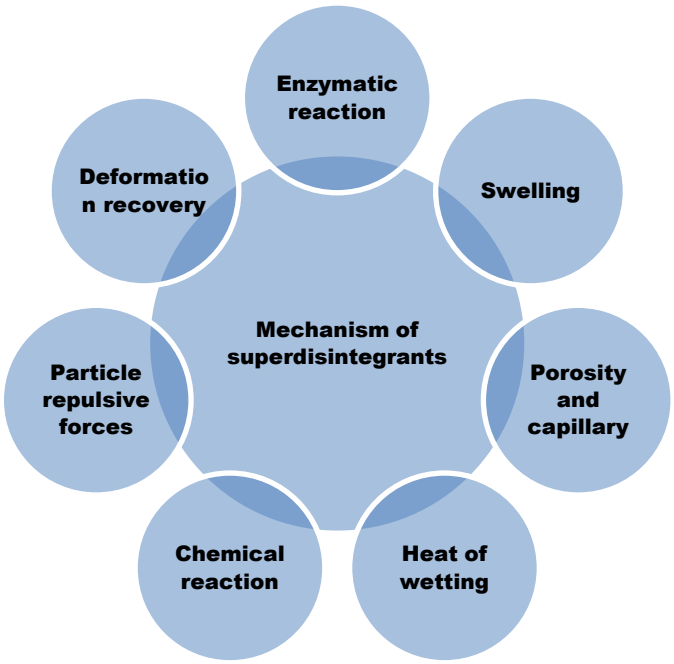

Fig. 2: Mechanism of superdisintegrants

Type of Superdisintegrant and their examples[4]

Table 2: Types of superdisintegrants

S. No.	Natural superdisintegrant	Synthetic superdisintegrant
1	These superdisintegranting agents are natural in origin and are preferred over synthetic substances. They are comparatively cheaper, abundantly available, non-irritating and nontoxic in nature.	Synthetic superdisintegrants are used in tablet formulations to break the tablet and to improve the rate and extent of tablet disintegration thereby increasing the rate of drug dissolution.
2	Advantages: Easy availability, cost effectiveness, Eco friendliness, emollient and non-irritant nature, non-toxicity, capable of multitude of chemical modifications, potentially degradable and compatible due to natural origin.	Advantages: Effective in lower concentrations than starch. Less effect on compressibility and flow ability. More effective intragranularly.

Table 3: Few examples of natural and synthetic superdisintegrants used in the formulation of fast dissolving tablets

S. No.	Natural superdisintegrants	Synthetic superdisintegrants
1	Locust bean gum	Crosspovidone
2	Fenugreek gum	Croscarmellose sodium
3	Banana powder	Sodium starch glycolate
4	Karaya gum	Calcium silicate
5	Gellan gum	Soy polysaccharides
6	Guar gum	

CHARACTERIZATION OF SUPERDISINTEGRANTS[5]

1. Swelling index

The study was carried out by using a 100 ml stoppered graduated cylinder. The initial bulk volume of 1 g of powder was noted. Water was added in sufficient quantity to ensure 25 ml of uniform dispersion by vigorously shaking every 10 min for 1 hour and then allowed to stand for 24 hour. The dispersion was stored at room temperature and the sediment volume of the swollen mass was measured after 24 hour.

Swelling index=100*(V2-V1/V1)

Where, V1=Initial volume of material before hydration; V2=Volume of hydrated material.

2. Viscosity

One gram of powder was suspended in 75 ml of distilled water for 4 h. Distilled water was added up to 100 ml to produce the concentration of 1%. The mixture was homogenized by mechanical stirrer for 2 h and its viscosity was determined by using Brookfield viscometer, spindle SC4-18 (Brookfield Viscometer, DV-2+LV) at 5 r/ min.

3. Loss on drying

Loss on drying technique is used to determine high levels of moisture or solvents present in the sample. The material sample was weighed (W1) and heated in an oven for 2 h. It was cooled in the dry atmosphere of desiccators and then finally weighed (W2).

% Loss on drying=[(W1-W2)/W1]*100

Where, W1=Initial weight of the powder; W2=Final weight of the powder.

4. pH

One gram of powder was suspended in 100 ml of distilled water and pH was checked by using digital pH meter.

5. Solubility

Solubility is determined by dissolving powder sample in the aqueous, organic and inorganic solvents.

EVALUATION TEST OF FAST DISSOLVING TABLETS[6]

A. Drugs and Excipients compatibility test

FT-IR Studies: Fourier transform Infrared spectroscopy (FT IR Spectrometer Bruker ALPHA) was employed to determine the compatibility of drug with the excipients. About 2 mg of pure drug and formulation were dispersed in potassium bromide powder and pellets were prepared by applying 6 tons pressure. The positions of FT-IR bands of important functional groups were identified and were mapped with FT-IR of drugs with formulation. The individual drug and the final formulation containing excipients were selected and scanned separately. Both the spectra were compared for confirmation of common peaks. The samples were scanned from ranges 400 to 4000 $cm^{-1.}$

B. Differential scanning calorimetry (DSC)

Differential scanning calorimetry was used to characterize thermal properties. The DSC thermograms were recorded using TA-60 thermal analyzer (Shimadzu) for all formulations. The samples were hermetically sealed in aluminium pans and heated at a constant rate of 20o /min over temperature range of 50 to 200^{o}. Inert atmosphere was maintained by purging nitrogen gas at flow rate of 50 ml/min.

C. Pre Compression Parameter

1. Angle of Repose

Angle of repose was determined by using funnel method. The blend was poured through funnel that can be raised vertically until a maximum cone height (h) was obtained. Radius of the heap was measured and angle of repose was calculated using the formula,

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

Where, Θ is the angle of repose, h is the height of pile r is the radius of the base of pile

2. Bulk density

Bulk density of a powder is defined as the ratio of the mass of the powder and its bulk volume. It is used to describe packing of particles. For bulk determination, a weighed quantity of the powder material was introduced into a graduated measuring cylinder and volume of powder was determined.

Bulk Density= Mass of the powder/ bulk volume

3. Tapped density

For determination of the tapped density, a weighed quantity of the powder was introduced into a graduated measuring cylinder and was tapped mechanically either manually or using a taping device till a constant volume was obtained.

Tapped Density= Mass of the powder/ tapped volume

4. Carr's compressibility index

The simplest way of measurement of free flow of powder is compressibility, an indication of the ease with which a material can be induced to flow. The compressibility index is determined by Carr's index, which is calculated by using the following formula,

$$C= 100(1-B/T)$$

Where, B is bulk density, T is tapped density

5. Hausner's Ratio

Hausner's ratio is an index of ease of powder flow. It is calculated by the following formula, Hausner's Ratio= Tapped density/ Bulk density Lower Hausner's ratio (< 1.25) indicates better flow properties than higher ones (>1.25)

D. Post Compression Parameter[7]

1. Hardness

The hardness of the tablet indicates its tensile strength and is measured in terms of load/pressure required to crush it when placed on its edge. Hardness has influence on disintegration and dissolution times and may affect bioavailability. Monsanto hardness tester was used to measure hardness of the formulated tablet. The tester consists of a barrel containing a compressed spring held between two plungers. The lower plunger was then forced against a spring by turning a threaded bolt until the tablet fractures. As the spring was compressed, a pointer rides along a gauge in the barrel to indicate the force. The force of fracture ease record and the zero force reading was deducted from it. It is expressed in kg/cm^2.

2. Friability

This test evaluates ability of tablet to withstand abrasion and edge damage during packing, handling and shipping. Friability generally reflects poor cohesion of tablet ingredients. Friability was measured by the help of Roche friabilator. 10 tablets were weighed and placed in plastic chamber that revolves at 25 rpm for 4 minutes. Tablets were reweighed after removal of fines. The friability was calculated by the formula-

$$F= w(initial)- w(final)/w(initial)$$

3. Weight variation

Tablets are designed to contain a specific amount of drug in a specific amount of tablet formulation. The weight of the tablet is measured to help ensure that a tablet contain the proper amount of drug. 20 tablets were selected randomly from each formulation were individually weighed using an electronic balance. Average weight of the tablets was calculated. The individual weight of the tablet was compared with average weight. The tablets meet the USP specification if not more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit.

$$\text{Weight variation} = wavg - winitial / wavg \times 100$$

4. Disintegration time

The process of breakdown of a tablet into smaller particles is known as disintegration. One tablet was placed in each of 6 tubes of the basket. A disc was added to each tube and the apparatus was run using 6.8pH phosphate buffer maintained at 370C as the immersion liquid. The assembly was raised and lowered between 30 cycles per minute in the 6.8pH phosphate buffer. The time in second taken for complete disintegration of the tablet with no mass remaining in the apparatus was measured and recorded. The tablet must be disintegrated within 3 minutes.

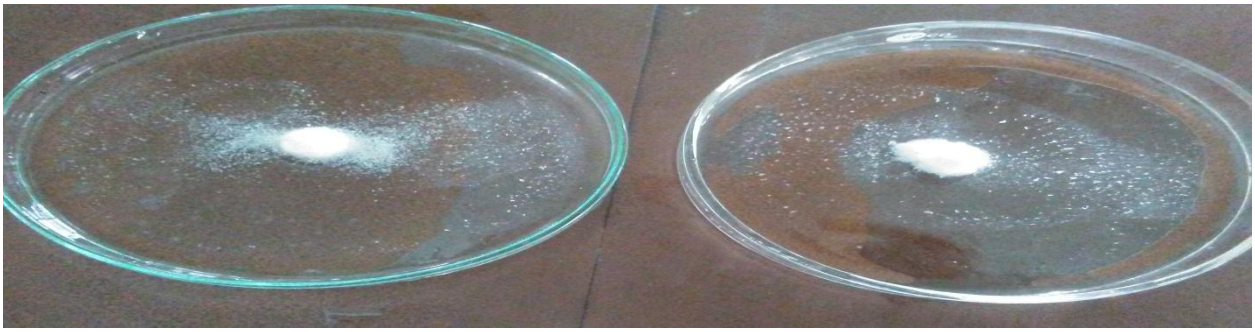

Fig. 3: Diagram showing *in vitro* disintegration time test

5. In vitro dissolution studies

In-vitro dissolution studies of the tablets were carried out in USP dissolution apparatus type IIby employing a paddle stirrer at 50 rpm using 900 ml of pH 6.8 phosphate buffer sat 37± 0.50C as a dissolution medium. One tablet was used in each test. Aliquots of 5 ml each were withdrawn at specified time intervals (0, 2, 6, 8, 10, and 12) and replaced with equal volume of fresh medium. The withdrawn aliquots were analyzed for drug content spectrophotometrically at required ʎmax. Drug concentration was calculated and expressed as cumulative percent of the drug released.

6. Wetting time

The significant parameters for Fast Dissolving Tablets are the ratio of wetting time and water absorption reported by Yunixia et al. A piece of filter paper folded twice (circularly cut) was placed in a small petri plate containing water soluble dye solution (Sorenson‟s buffer pH 6.8). Tablet was placed in the paper, and the time required for complete wetting of the tablet was determined. Three trials for each batch and the standard deviation were also determined.

Fig. 4: Wetting time test

7. Drug content

Twenty tablets were weighed and powdered. The quantity of powder equivalent to 50 mg of drug was dissolved in phosphate buffer pH 6.8 diluted to 100 ml with the same and the solution was filtered and suitably diluted. The drug content was estimated spectrometrically at required wavelength.

8. *Invitro* dispersion time

Tablet was added to 10 ml of phosphate buffer solution, pH 6.8 at 37+0.5ºC, Time required for complete dispersion of a tablet was measured.

9. Moisture uptake studies

Moisture uptake studies for FDT should be performed to check the stability of the formulation. Ten tablets from each formulation were kept in a desiccator over calcium chloride at 37c for 24 hour and then they were weighed and exposed to 75% RH, at room temperature for 2 weeks. One tablet as control (without superdisintegrants) was kept to assess the moisture prescence due to the other excipients. All the tablets were weighed and the percentage increase in weight was recorded.

Table 4: Some marketed available product of fast dissolving tablets

S. No.	Products	Manufacturer
1	Torrox MT	Torrent Pharmaceuticals, India
2	Olanexinstab	Ranbaxy Labs Ltd., New Delhi,
3	Fast & up	Aeronutrix
4	Liecet-MD	Mitshealthcare, Haryana
5	Prozotil- MD	Lifecare neuro product limited

CONCLUSION

In this busy world, an individual desires that everything should be easily accessible. In consideration with health, fast dissolving drug delivery system provides an easiest administration of dosage form without the need of water. Fast dissolving tablets is beneficial for all age groups pediatrics, gediatics, travelling personnel, unconscious patients, athletes, etc. Fast dissolving tablets overcomes the drawbacks of the conventional dosage forms and thus getting more popularity and importance in the pharmaceutical industries. Hence, researchers and scientists are more concerning to develop and innovate the best and simple version of this dosage form to treat all kinds of serious and emergency disorders like convulsions, cardiac arrest, asthma attack, etc to prevent the life of an individuals.

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