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FAST DISSOLVING TABLETS AS A NOVEL VITAL CONCEPT: A REVIEW

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Abstract: Tablets are amongst the most traditional and ancient oral dosage forms. There are several recent developments in technology have presented viable dosage alternatives for patients who may have difficulty swallowing tablets or liquids. Traditional tablets and capsules administered with an 8-oz. glass of water may be inconvenient or impractical for some patients. Due to that, the target populations for these new fast-dissolving/disintegrating dosage forms have generally been pediatric, geriatric, and bedridden disabled patients. Patients with persistent nausea, who are traveling, or who have little or no access to water are also candidates for FDDTs. Oral drug delivery remains the preferred route for administration of various drugs. Recent developments in the technology have prompted scientists to develop orally fast disintegrating tablets with improved patient compliance and convenience. FDTs are solid unit dosage forms, which disintegrate or dissolve rapidly in the mouth without chewing and water. Such tablets provide several advantages particularly for pediatric and geriatric populations. This review deals with the recent advances on the fast dissolving tablets and thorough information regarding every aspect of fast disintegrating tablets, such as disintegrants employed and technologies developed for FDTs, along with various excipient, evaluation tests, marketed formulations, and drugs explored in this field.

Keywords: Disintegration, fast dissolving tablets, pediatrics, geriatrics, oral drug delivery



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INTRODUCTION

Tablet is the most popular among all dosage forms existing today because of its convenience of self administration, compactness and easy manufacturing. According to European Pharmacopoeia, the fast dissolving tablets should disperse/disintegrate in less than three minutes. The basic approach used in development of fast dissolving tablets (FDT) is the use of superdisintegrants like Cross linked carboxymethylcellulose (Croscarmellose), Sodium starch glycolate (Primogel, Explotab), Polyvinylpyrrolidone (Polyplasdone) etc. which provide instantaneous disintegration of tablet as soon as kept over the tongue and release the drug in saliva. The bioavailability of some drugs may be increased 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. Moreover, the amount of drug that is subject to first pass metabolism is reduced as compared to standard tablets.

Fast Dissolving Tablets: The Center for Drug Evaluation and Research (CDER), US FDA defined Oral Disintegrating Tablets (ODT) as “A solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue.” A fast-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; repi melts, porous tablets, oro-dispersible, quick dissolving or rapid disintegrating tablets.

Following are the characteristics of Fast-Dissolving Tablets

- Ease of administration for uncooperative patients who are mentally or physically disabled.
- Requires no water.
- Quick disintegration and dissolution of the dosage form.
- Overcomes unacceptable taste of the drugs and also to provide a pleasant mouth feel.
- Can be designed to leave minimal or no residue in the mouth after administration.
- Allows high drug loading.
- Ability to provide advantages of liquid medication in the form of solid preparation.
- Adaptable and amenable to existing processing and packaging machinery.
- Cost-effective.

Challenges occurs in formulating Fast disintegrating tablets

- Palatability
- Mechanical strength
- Hygroscopicity
- Amount of drug
- Aqueous solubility
- Size of tablet

Salient Features of Fast Dissolving Drug Delivery System

- Ease of administration in accurate dose.
- No need of water to swallow the dosage form.
- Convenience of administration.
- Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach; in such cases bioavailability of drugs is increased.
- Good mouth feels properly of MDDS helps to change the basic view of medication as "bitter pill", particularly for paediatric patients.
- Rapid dissolution of drug and absorption which may produce rapid, onset of action.
- Ability to provide advantages of liquid medication in the form of solid preparation.
- Pregastric absorption can result in improved bioavailability and as a result of reduced dosage, improved clinical performance through a reduction of unwanted effects.

Following are the advantages of fast dissolving tablets:

- Quick onset of action and improved bioavailability.
- Useful for patients who cannot swallow the dosage forms and for pediatric, geriatric and mentally retard patients.
- Improved patient compliance.
- Frequently administered when water is not available.

- Accurate dose can be given as compared to oral liquids.
- Pleasant mouth feel of the tablet helps to change the perception of medication as bitter pill particularly in pediatric patients.
- Allow high drug loading.
- Stability of drug is improved as compared to oral dosage forms like suspensions.
- Disintegrates rapidly which may result in rapid release of drugs.
- High production capacity as compared to suspensions.

Excipients used in formulation of fast dissolving tablets: Excipients balance the properties of the actives in fast-melting tablets. This demands a thorough understanding of the chemistry of these excipients to prevent interaction with the actives. Determining the cost of these ingredients is another issue that needs to be addressed by formulators. The role of excipients is important in the formulation of fast-melting tablets.

- **Bulking Materials:** (as diluent, filler and cost reducer) Mannitol, polydextrose, lactitol, DCL (direct compressible lactose) and starch hydrolysate for higher aqueous solubility and good sensory perception.
- **Emulsifying Agents:** Alkyl sulfates, propylene glycol esters, lecithin, sucrose esters and others. These agents can be incorporated in the range of 0.05 percent to about 15 percent by weight of the final composition.
- **Lubricants:** Lubricants, though not essential excipient, enhance palatability after they disintegrate in the mouth.
- **Flavours and Sweeteners:** Sugar, dextrose and fructose, as well as non-nutritive sweeteners such as aspartame, sodium saccharin, sugar alcohols and sucralose. The addition of sweeteners contributes a pleasant taste as well as bulk to the composition.
- **Super Disintegrants:** A disintegrant is an excipient, which is added to a tablet or capsule blend to aid in the breakup of the compacted mass when it is put into a fluid environment. Its Advantages are :
 - Effective in lower concentrations.
 - Less effect on compressibility and flow ability.
 - More effective intragranularly.

Examples of super disintegrants are:

- Sodium Starch Glycolate (Explotab, primogel) used in concentration of 2-8 % & optimum is 4%.
- Cross-linked Povidone (crospovidone) , (Kollidone) used in concentration of 2-5% of weight of tablet.
- Low-substituted hydroxyl propyl cellulose, concentration 1-5%
- Cross linked carboxy methyl cellulose sodium (i.e. Ac-Di-sol) Croscarmellose sodium: 1-3%
Direct Compression
- Gas producing disintegrants

Mechanisms of fast dissolving tablets: To achieve the tablets fast dissolving properties:

- Water must quickly enters into the tablet matrix to cause rapid disintegration and instantaneous dissolution of the tablet.
- Incorporation of an appropriate disintegrating agent or highly water soluble excipients in the tablet formulation.
- There are some undermentioned mechanisms by which the tablet is broken down into the smaller particles and then subsequently result a solution or suspension of the drug. The mechanisms are:
 - High swellability of disintegrants
 - Chemical reaction
 - Capillary action

Conventional techniques used for preparation of fast dissolving tablets:

- **Disintegrant Addition:** Disintegrant addition technique is one popular techniques for formulating Fast-dissolving tablets because of its easy implementation and cost-effectiveness. The basic principle involved in formulating Fast-dissolving tablets by disintegrant addition technique is addition of superdisintegrants in optimum concentration so as to achieve rapid disintegration along with the good mouth feel.
- **Freeze Drying:** A process in which water is sublimated from the product after freezing. Lyophilization is a pharmaceutical technology which allows drying of heat sensitive drugs

and biological at low temperature under conditions that allow removal of water by sublimation. Lyophilization results in preparations, which are highly porous, with a very high specific surface area, which dissolve rapidly and show improved absorption and bioavailability.

- **Moulding:** Molded tablets are prepared by using water-soluble ingredients so that the tablets dissolve completely and rapidly. The powder blend is moistened with a hydro-alcoholic solvent and is molded into tablets under pressure lower than that used in conventional tablet compression. The solvent is then removed by air-drying. Molded tablets are very less compact than compressed tablets. These possess porous structure that enhances dissolution.
- **Sublimation:** The slow dissolution of the compressed tablet containing even highly water-soluble ingredients is due to the low porosity of the tablets. Inert solid ingredients volatilize readily such as (e.g. Urea, ammonium carbonate, ammonium bicarbonate, hexa methylene tetramine, camphor etc.) , were added to the other tablet ingredients and the mixture is compressed into tablets. The volatile materials were then removed via sublimation, which generates porous structures. Additionally, several solvents (e.g. cyclohexane, benzene) can be also used as pore forming agents,
- **Spray-Drying:** Spray drying can produce highly porous and fine powders that dissolve rapidly. The formulations are incorporated by hydrolyzed and non hydrolyzed gelatins as supporting agents, mannitol as bulking agent, sodium starch glycolate or crosscarmellose sodium as disintegrating and an acidic material (e.g. citric acid) and / or alkali material (e.g. sodium bicarbonate) to enhance disintegration and dissolution. Tablet compressed from the spray dried powder disintegrated within 20 seconds when immersed in an aqueous medium.
- **Mass-Extrusion:** 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 of the product into even segments using heated blade to form tablets. The dried cylinder can also be used to coat granules of bitter tasting drugs and thereby masking their bitter taste.
- **Direct Compression:** It is the easiest way to manufacture tablets. Conventional equipment, commonly available excipients and a limited number of processing steps are involved in direct compression. Also high doses can be accommodated and final weight of tablet can easily exceed that of other production methods. Disintegration and solubilization of directly compressed tablet's depends on single or combined action of disintegrants, water soluble excipients and effervescent agent.

Patented Technologies for Fast Dissolving Tablets

1. Zydis technology
2. Lyoc
3. Quick solv
4. Nanocrystal technology
5. Flashtab technology
6. Orasolv technology
7. Durasolv technology
8. WOW tab technology
9. Dispersible tablet technology
10. Pharmaburst technology
11. Frosta technology
12. Oraquick
13. Ziplelets/advatab

Parameters employed for evaluation of fast dissolving tablets:

Evaluation of Blends: 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:

Angle of repose: The angle of repose was determined by the funnel method suggested by Newman. Angle of repose is determined by the following formula $\tan\theta = hr$

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

Where θ = Angle of repose

Bulk density: Density is defined as weight per unit volume. Bulk density, ρ_b , is defined as the mass of the powder divided by the bulk volume and is expressed as $\rho_b = MV$

Where ρ_b = Bulk Density

Bulkiness: Specific bulk volume or reciprocal of bulk density is called bulkiness or bulk. The bulkiness can be calculated by the following formula Bulkiness= $1/P_b$

Where, P_b = Bulk Density.

Loose bulk density: ρ_u = Weight in grams / V_b

Where V_b = Bulk volume (untapped volume)

Void Volume: The volume of the spaces is known as the void volume "V" and is given by the formula.

$$V = V_b - V_p$$

Where V_b = Bulk volume (volume before tapping)

V = True volume (volume after tapping)

Porosity: The porosity ϵ 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:

$$\epsilon = \frac{V_b - V_p}{V_b}$$

Porosity is frequently expressed in percentage and is given as

$$\% \epsilon = \left(1 - \frac{V_p}{V_b}\right) \times 100$$

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

$$\%C = \frac{P_b - P_u}{P_b} \times 100$$

Evaluation of Fast Dissolving Tablet: Tablets from all the formulation were subjected to following quality control tests

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.

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. Ten tablets were taken and their thickness was recorded using micrometer.

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.

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.

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

$$\% \text{ Friability} = \frac{\text{Loss in weight}}{\text{Initial weight}} \times 100$$

In-Vitro disintegration test: The test was carried out on 6 tablets using the apparatus specified in I.P.-1996 distilled water at $37^{\circ}\text{C} \pm 2^{\circ}\text{C}$ was used as a disintegration media and the time in second taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured in seconds.

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.

Stability testing of drug: (temperature dependent stability studies):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 at; $40 \pm 1^\circ\text{C}$, $50 \pm 1^\circ\text{C}$, $37 \pm 1^\circ\text{C}$ and RH $75\% \pm 5\%$. The tablets were withdrawn after a period of 15 days and analyzed for physical characterization (Visual defects, Hardness, Friability, Disintegrations, and Dissolution etc.) and drug content. The data obtained is fitted into first order equations to determine the kinetics of degradation. Accelerated stability data are plotting according Arrhenius equation to determine the shelf life at 25°C .

Packaging: Expensive packaging, specific processing, and special care are required during manufacturing and storage to protect the dosage of other fast-dissolving dosage forms. Unlike these other quick-dispersing and/or dissolving oral delivery systems, the system can be packaged using various options, such as single pouch, blister card with multiple units, multiple-unit dispenser, and continuous roll dispenser, depending on the application and marketing objectives.

Table.1. Marketed Fast Dissolving Tablets in India

Name of the Product	Active ingredients
Imodium Lingual	Imodium
Nimulid-MD	Nimesulide
Mosid-MT	Mosapride citrate
Zyrof Meltab	Rofecoxib
Pepcidin Rapitab	Pepcid
Claritin Reditab	Micronized Loratidine

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