A REVIEW ON FAST DISSOLVING TABLET

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ABSTRACT
Although marvelous advancement in drug delivery, oral route remains the preferred route for the administration due to higher levels of patient compliance. Tablet is the most popular among all oral dosage forms existing today because of recently, fast-dissolving drug delivery systems have started gaining popularity and acceptance as new drug delivery systems, because they are easy to administer and lead to better patient compliance its convenience of self administration, compactness and easy manufacturing; however hand tremors, dysphasia in case of geriatric patients, the underdeveloped muscular and nervous systems in young individuals and in case of uncooperative patients, the problem of swallowing is common phenomenon which leads to poor patient compliance. To overcome these drawbacks, mouth dissolving tablets (MDT) or orally disintegrating tablets; (ODT) has emerged as alternative oral dosage forms. These are novel types; of tablets that disintegrate/dissolve/ disperse in saliva within few seconds’. According to European Pharmacopoeia, the ODT should disperse/disintegrate in less than three minutes. The basic approach used in development of MDT is the use of superdisintegrants like Cross linked carboxymethylcellulose (Croscarmeliose), Sodium starch glycolate (Primogel, Explotab). Polyvinylpyrrolidone (Polyplasdone) etc. which provide instantaneous disintegration of tablet after putting on tongue, thereby releasing 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 the standard tablets.

Keywords: Fast Dissolving Tablet, Direct compression, Super-disintegrants, Lyophilization.

INTRODUCTION
A fast-dissolving drug delivery system, in most cases, is a tablet that dissolves or disintegrants in the oral cavity without the need of water or chewing. Most fast-dissolving delivery system films must include substances to mask the taste of the active ingredient. This masked active ingredient is then swallowed by the patient’s saliva along
with the soluble and insoluble excipients. These are also called melt-in-mouth tablets, porous tablets, oro-dispersible, quick dissolving or rapid disintegrating tablets \(^1\).

**ADVANTAGES OF FDT**

Administration to the patients who cannot swallow, such as the elderly, stroke victims, bedridden patients, patients affected by renal failure & patients who refuse to swallow such as pediatric, geriatric & psychiatric patients. It achieve increased bioavailability/rapid absorption through pregastric absorption of drugs from mouth, pharynx & oesophagus as saliva passes down. It was convenient for administration and patient compliance 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 & the risk of choking or suffocation during oral administration \(^3\).

**SELECTION OF DRUGS**

The ideal characteristics of a drug for in vivo dissolution from an FDT include

1. No bitter taste
2. Dose lower than 20mg
3. Small to moderate molecular weight
4. Good stability in water and saliva
5. Partially non ionized at the oral cavities pH
6. Ability to diffuse and partition into the epithelium of the upper GIT (log P>1, or preferably>2)
7. Ability to permeate oral mucosal tissue

Unsuitable drug characteristic for FDT;

1. Short half-life and frequent dosing
2. Very bitter or otherwise unacceptable taste because taste masking cannot be achieved
3. Required controlled or sustained release
To overcome these drawbacks, mouth dissolving tablets (MDT) or orally disintegrating tablets; (ODT) has emerged as alternative oral dosage forms. These are the unique type of tablets that disintegrate or dissolve or disperse in salivary fluid within few seconds'. According to official publication European Pharmacopoeia the ODT should be disperses or disintegrates in less than three minutes. The fundamental approach used in development of ODT is the use of superdisintegrants like Sodium starch glycolate, (Primogel, Explotab) carboxymethylcellulose (Crocarmeliose). Polyvinylpyrrolidone (Polylondone) etc. which provides rapid disintegration of tablet after putting in mouth, and release the drug in saliva. Bioavailability of certain drugs may be increased due to absorption of drugs in oral cavity and may be due to pregastric absorption of saliva which contains dispersed drugs which pass down into the stomach. The amount of drug which is subject to undergo first pass metabolism is reduced [4].

BIOPHARMACEUTICAL CONSIDERATION

When new drug delivery system put on, it is must that to consider Biopharmaceutical factor like metabolism and excretion.

Pharmacokinetics:

Study has done on absorption, distribution, metabolism and excretion in this consideration. Drug attains therapeutic level after absorption and therefore elicits pharmacological effect, so both rate and extend of absorption is important. There is delay in disintegration and therefore dissolution in conventional dosage form while FDTs is rapidly disintegrates in oral cavity and dissolution is rapid. Due to disintegration of FDTs in mouth absorption in started from mouth, pharynx and esophagus. Some factors like age, GI pH, and blood flow through GI are taken into consideration, because elders may be considered as separate unique Medicare population. There are many factors on which drug distribution depends like tissue permeability, perfusion rate, binding of drug to tissue, disease state, drug interaction etc. In geriatric patients, decrease in body mass and total body water result in decreased volume of distribution of water-soluble drugs and increased volume of distribution of lipid soluble drugs. Duration and intensity of action
depends upon rate of drug removal from the body or site of action i.e. biotransformation. Decrease in liver volume, regional blood flow to liver reduces the biotransformation of drug through oxidation, reduction and hydrolysis. Excretion by renal clearance is slowed, thus half-life of renal excreted drugs increase.

**Pharmacodynamics:**

Drug receptor interaction impaired in elderly as well as in young adult due to undue development of organ. Decreased ability of the body to respond baro reflexive stimuli, cardiac output, and orthostatic hypotension may see in taking antihypertensive like prazosin thus decreased sensitivity of the CVS to β-adrenergic agonist and antagonist. Immunity is less and taken into consideration while administered antibiotics. Altered response to drug therapy-elderly show diminished bronchodilator effect of theophylline shows increased sensitivity to barbiturates. Concomitant illnesses are often present in elderly, which is also taken into consideration, while multiple drug therapy prescribed. Research workers have clinically evaluated drug combination for various classes of drug like cardiovascular agents, diuretics, anti-hypertensive in geriatrics. The combination choice depends on disease state of the patient [5].

**CHALLENGES IN FORMULATION OF FAST DISINTEGRATING TABLETS (FDTS)**

1. **Mechanical strength and disintegration time:**

   It is obvious that increasing the mechanical strength will delay the disintegration time. So a good compromise between these two parameters is always essential. FDTs are formulated to obtain disintegration time usually less than a minute. While doing so, maintaining a good mechanical strength is a prime challenge [9].

2. **Taste masking:**

   As most drugs are unpalatable, rapid disintegrating drug delivery systems usually contain the medicament in a taste-masked form. Delivery systems disintegrate or dissolve in patients oral cavity, thus releasing the active ingredients which come in contact with the taste buds; hence, taste-masking of the drugs becomes essential to patient compliance [10].
3. Aqueous solubility:
Water-soluble drugs pose various formulation challenges because they form eutectic mixtures, which result in freezing-point depression and the formation of a glassy solid that may collapse upon drying because of loss of supporting structure during the sublimation process and it can be prevented by using various matrix-forming excipients such as mannitol which, have ability to induce crystallinity and hence, impart rigidity to the amorphous composite \[^{[11]}\].

4. Hygroscopicity:
Several orally disintegrating dosage forms are hygroscopic and cannot maintain physical integrity under normal conditions of temperature and humidity. Hence, they need protection from humidity which calls for specialized product packaging. \[^{[12]}\]

5. Amount of drug:
The application of technologies used for FDTs is limited by the amount of drug that can be incorporated into each unit dose. For lyophilized dosage forms, the drug dose must be lower than 400 mg for insoluble drugs and less than 60 mg for soluble drugs. This parameter is particularly challenging when formulating a fast-dissolving oral films or wafers \[^{[13]}\].

6. Size of tablet:
It has been reported that the easiest size of tablet to swallow is 7-8 mm while the easiest size to handle was larger than 8 mm.
Therefore, the tablet size that is both easy to take and easy to handle is difficult to achieve \[^{[13]}\].

7. Mouth feel:
FDTs should not disintegrate into larger particles in the oral cavity. The particles generated after disintegration of the FDTs should be as small as possible. Moreover addition of flavors and cooling agents like menthol improve the mouth feel \[^{[13, 14]}\].
8. Sensitivity to environmental conditions: FDTs should exhibit low sensitivity to environment conditions such as humidity and temperature as most of the materials used in FDTs are meant to dissolve in minimum quantity of water\(^{[14]}\).

**METHODS USED FOR PREPARATION OF FAST DISSOLVING TABLET**

1. **Disintegrant Addition**

   Disintegrant addition technique is one of 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. Microcrystalline cellulose and low substituted hydroxypropylcellulose were used as disintegrating agents in the range of 8.2 – 9.1 to prepare fast dissolving tablet. Agar powder is used as disintegrant for the development of rapidly disintegration tablets by enhancing the porosity of agar by water treatment. Rapidly disintegrating tablets of bitter drugs oxybutynin & pirenzepine were prepared by using the taste masked granules and h mixture of excipients consisting of crystalline cellulose (Avicel PH 0-2) and low-substituted hydroxypropy cellulose HPC, LH-11),

2. **Freeze Drying**

   It is 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.
3. Moulding

Tablet produced by molding are solid dispersion. Molded tablets disintegrate more rapidly and offer improved taste because the dispersion matrix is generally made from water soluble sugars. The active ingredient in most cases is absorbed through the mucosal lining of the mouth. The manufacturing process of molding tablets involves moistening the powder blend with a hydro alcoholic solvent followed by pressing into mold plates to form a wetted mass (compressing molding). The solvent is then removed by air drying. Thus the process is similar to what is used in the manufacture of tablet triturates. Such tablets are less compact than compressed tablets and possess a porous structure that hastens dissolution. Molded forms are also prepared using a heat-molding process that involves setting the molten mass that contains a dispersed drug. The heat-molding process uses an agar solution as a binder and a blister packaging well as a mold to manufacture a tablet. The process involves preparing a suspension that contains a drug, agar, and sugar (e.g., mannitol or lactose), pouring the suspension into the blister packaging well, solidifying the agar solution at room temperature to form a jelly, and drying at -300C under vacuum. Another process used is called no-vacuum lyophilisation,
which involves the evaporation of a solvent from a drug solution or suspension at standard pressure.

4. 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.

5. 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 \[15, 16\].

6. 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.

7. Sublimation

Because of low porosity, compressed tablets composed of highly water-soluble excipients as tablet matrix material often do not dissolve rapidly in the water. Porous tablets that exhibit good mechanical strength and dissolve quickly have been developed by Heinnemann & Rose, et al \[24\]. Inert solid ingredients (ex. urea, urethane, ammonium carbonate, camphor, naphthalene) were added to other tablet excipients and the blend was compressed into tablet. Removal of volatile material by sublimation generated a porous structure.
EXCIPIENTS COMMONLY USED FOR ODT PREPARATION

It contains active principle, mixture of excipients comprising at least one disintegrant, a diluent, a lubricant, and, optionally, a swelling agent, a permeabilizing agent, sweeteners, and flavorings.

**TABLE 1: NAME AND WEIGHT PERCENTAGE OF DIFFERENT EXCIPIENTS**

<table>
<thead>
<tr>
<th>Name of Excipient</th>
<th>Percentage used</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disintegrant</td>
<td>1 to 15%</td>
</tr>
<tr>
<td>Diluent</td>
<td>0 to 85%</td>
</tr>
<tr>
<td>Binder</td>
<td>5 to 10%</td>
</tr>
<tr>
<td>Antistatic agent</td>
<td>0 to 10%</td>
</tr>
</tbody>
</table>

EVALUATION OF FAST DISINTEGRATING TABLETS

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 overall "elegance" is essential for consumer acceptance and 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. **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.

5. **Friability (F):** Friability of the tablet determined using Roche friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at height of 6 inches in each revolution. Pre-weighted sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. The friability (F) is given by the formula.

\[
F = W^{int} - W^{fin}
\]

Where, \( W^{int} \) - Weight of tablets before friability.

\( W^{fin} \) - Weight of tablets after friability.

6. **Wetting Time:** Wetting time of dosage form is related to the contact angle. It needs to be assessed to give an insight into the disintegration properties of the tablets; a lower wetting time implies a quicker disintegration of the tablet. For this purpose, a tablet is placed on a piece of tissue paper folded twice and kept in a small Petri dish (ID = 6.5 cm) containing 6 ml of water, and the time for complete wetting is measured.

7. **Water absorption Ratio:** A piece of tissue paper folded twice was placed in a small Petridish containing 6 ml of water. A tablet was put on the paper & the time required for
complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio, R, was determined using following equation,

$$R = 10 \left( \frac{w_a}{w_b} \right)$$

Where, $w_a$ is weight of tablet before water absorption & $w_b$ is weight of tablet after water absorption.

8. 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. In vitro Dissolution test: The development of dissolution methods for FDTs is comparable to the approach taken for conventional tablets and is practically identical. Dissolution conditions for drugs listed in a pharmacopoeia monograph, is a good place to start with scouting runs for a bioequivalent FDT. Other media such as 0.1 M HCl and buffer (pH 4.5 and 6.8) should be evaluated for FDT much in the same way as their ordinary tablet counterparts. It has been suggested that USP 2 paddle apparatus is the most suitable and common choice for orally disintegrating tablets, with a paddle speed of 50 rpm commonly used.

10. Stability testing of drug (temperature dependent stability studies): The fast disintegrating tablets are packed in suitable packaging and stored under the following conditions for a period as prescribed by ICH guidelines for accelerated studies.

(1) 40 ± 1 °C
(2) 50 ± 1°C
(3) 37 ±1 °C and RH 75% ± 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.
11. Packaging: Packing is one of the important aspects in manufacturing FDT. The products obtained by various technologies vary in some of the parameters especially in mechanical strength to a good extent. The products obtained by lyophilization process including various technologies such as Zydis, Lyoc, Quicksolv, and Nanocrystal are porous in nature, have less physical resistance, sensitive to moisture, and may degrade at higher humidity conditions. For the above reasons products obtained require special packing. Zydis units are generally packed with peelable backing foil. Paksolv is a special packaging unit, which has a dome-shaped blister, which prevents vertical movement of tablet within the depression and protect tablets from breaking during storage and transport, which is used for Orasolv tablet. Some of the products obtained from Durasolv, WOW Tab, Pharmaburst oraquick, Ziplets, etc. technologies have sufficient mechanical strength to withstand transport and handling shock so they are generally packed in push through blisters or in bottles [30, 31].

A PROMISING FUTURE

Oral delivery is currently the gold standard in the pharmaceutical industry where it is regarded as the safest, most convenient and most economical method of drug delivery having the highest patient compliance. The tablet is the most widely utilised oral dose format. A novel tablet concept which offers ease of oral administration and benefits of increased patient compliance is the ODT. This tablet format is designed to allow administration of an oral solid dose form in the absence of water or fluid intake. Such tablets readily dissolve or disintegrate in the saliva generally within <60 seconds. A number of ODT are commercially available for human use using technologies developed by pharmaceutical companies such as Cardinal Healthcare, Jannsen Pharmaceutical, Bioavail, and Eurand, Yamanouchi. However, these technologies use either expensive processing technology producing fragile tablets that require costly specialised packaging or use conventional tableting procedures which give longer than desired disintegration & still require specialised packaging. [33,34]
CONCLUSION

Fast dissolving tablets constitute an innovative dosage form, which overcomes the problem of swallowing and provides a quick onset of action. The paediatric and geriatric populations are the primary targets, as both the groups found it difficult to swallow conventional tablets. The basic approach followed by all the currently available technologies engaged in the formulation of Fast dissolving tablets is to maximize the porous structure of the tablet matrix and incorporate super disintegrating agents in optimum concentration so as to achieve rapid disintegration and instantaneous dissolution of the tablet along with good taste masking properties and excellent mechanical strength. The availability of the various technologies and manifold advantages of Fast dissolving tablets will surely increase its popularity in the near future.

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