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A Review on Oral Disintegrating Tablets: A New Perspective in Drug Delivery System

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ABSTRACT

The most prescribable and appropriate route in terms of patient's compliance is the delivery of drug by the oral route. Improving patient compliance always presents a challenge for developing an oral drug delivery system. Over the last decade, fast disintegrating tablets (FDTs) have received ever-increasing demand, and the field has become a rapidly rising pharmaceutical industry. Fast dissolving tablet are disintegrating and dissolve rapidly in the saliva without the need for water. Such tablets readily in the saliva dissolve or disintegrate in the saliva generally within < 60 seconds. Generally, superdisintegrants are used in the solid dosage form at a low concentration, typically 1-10% by weight relative to the total dosage unit weight, Different types of superdisintegrants such as synthetic, semi-synthetic, natural and co-processed blends, etc., have been used to establish successful mouth dissolving tablets and to resolve the limitations of traditional methods of tablet dosing. FDTs have benefits such as accurate dosing, easy portability, and manufacturing good physical and chemical stability and an ideal alternative for pediatric and geriatric patients. In addition to these benefits, dysphagia is the most common disadvantage of FDTs benefits associated with numerous conditions such as sudden allergy exposure, mental disability, motion sickness, unconsciousness, water unavailability etc. To get rid of these problems several innovative drug delivery systems have been developed like mouth dissolving tablet (MDTs). This article aims to address ideal properties, advantages, disadvantages, need for the formulation, superdisintegrants, patented technologies and evaluation and FDTs.

INTRODUCTION

The oral route remains the favored route for administration of therapeutic agents thanks to accurate dosage, low-cost therapy, self-medication, low-cost therapy, self-medication, non invasive method and straightforward administration leading to high level of patient compliance. [1] These are novel types of tablets that disintegrate/disperse/dissolve in saliva within few seconds without water. According to European pharmacopoeia, these MDTs should dissolve/disintegrate in less than three minutes. Mouth dissolving tablet is also called as orodispersible tablet, fast disintegration tablets, orally disintegration tablet, quick melt tablet, rapid melt tablets, porous tablet, However, of all the above terms United states pharmacopoeia (USP) approved these dosage forms as an ODTs. United States Food and Drug Administration (FDA) defined ODTs as "A solid dosage form containing medical substances or active ingredients which disintegrate rapidly within a few seconds when placed up on tongue". [2]

Oral administration of drug is preferred due to its ease of swallowing, distress avoidance, versatility and most significantly, patient compliance. The large number of patients find it difficult to swallow tablets and capsules, and do not take their medicines as prescribed. It is estimated that 50% of the papulation affected by this problem, which finally result in higher chance noncompliance and ineffective therapy. For these reasons, tablet that can disintegrate in the oral cavity, have attracted enormous attention. Solid dosage forms as oral tablets have the most considerable place among the entire pharmaceutical formulation. [5] Taste masking is the crucial step in the formulation of acceptable fast disintegrating/dissolving tablet (FDA). Traditional tablet formulation generally does not solve the issues related to the masking because it is supposed that the dosage form will not disintegrate until it passes through oral cavity. To eliminate the bitterness, the tablet can be prepared by adding flavors and sweetening agent or by sugar coating on the tablets. Many FDDT technology combine unique types of taste masking as well [3]. traditional tablets and capsules administered with a glass of water maybe inconvenience or impractical for some geriatric patients because of changes in various physiological and neurological condition associated with aging including difficulty in swallowing/dysphagia, memory, risk of chocking in addition to change in taste and smell. Solid dosage form also presents significant administration challenges in other patient groups, such as children, mentally challenged, bed ridden and uncooperative patients. Pediatrics patients may suffer from ingestion problems as a result of underdeveloped muscular and

nervous control. Moreover, patients travelling with little or no access to water, limit utility of orally administered conventional tablets or capsules. [4].

Advantages of oral dispersing tablets (ODTs)

The advantages of ODTs include. [3]

- No need of water to swallow the tablet.
- Compatible with taste masking and have a pleasing mouth feel.
- Can be easily administered to pediatric, elderly and mentally disabled patients.
- No residue in the oral cavity after administration.
- Manufacturing of the tablets can be done using conventional processing and packing equipment at minimum cost.
- Allow high drug loading.
- Accurate dose can be given as compared to liquids.
- Dissolution and absorption of the drug is fast, offering rapid onset of action.
- Advantageous over liquid medication in terms of administration as well as transportation
- ODTs or suitable for sustained and controlled release actives.

Limitation of ODTs [5,6]

- The major disadvantages of ODTs is related to the mechanical strength of tablets.
- Bad taste drugs are difficulty to formulate as an ODTs.
- Several FDT are hygroscopic cannot maintain the physical integrity under normal condition from humidity which requires specialized package.
- Dryness of the mouth due to decreased saliva production may not be good candidates for these tablet formulations.
- Rate absorption from saliva solution and overall bioavailability.
- Drug and dosage form stability.
- Mouth feels.

- If the tablet not properly formulated it may leave unpleasant taste.

Difficulties with Existing Oral Dosage Form [7]

1) Patient may suffer from tremors therefore they may have difficulty to take powder and liquids. In dysphagia physical obstacle and adherence to an esophagus may cause gastrointestinal ulceration.

2) Swallowing of solid dosage forms like tablet and capsule and produce difficulty for young adult of incomplete development of muscular and nervous system and elderly patient suffer from dysphagia.

3) Liquid medicaments (suspension and emulsion) are packed in multidose container; therefore, achievement of uniformity in the content of each dose may difficult.

4) Buccal and sublingual formation may cause irritation to oral mucosa, so patients refused to use such medication.

Challenges in the formulation of ODTs [3]

✓ Mechanical strength and disintegration time: Disintegration time will extend if the mechanical strength is more, so a good cooperation between these two kinds of parameter is necessary.

✓ Taste masking: Efficient taste masking of the bitter drugs must be done so that taste of the drug is not felt in the oral cavity.

✓ Mouth feels: The particle produced after disintegration of the ODT should be very small. ODT should not leave any residence in the mouth after oral administration. Addition of flavors and cooling agents like menthol enhance the mouth feel.

✓ Cost: The technology adopted for ODT should be acceptable in terms of cost of the final product.

Newer manufacturing technologies used now days for ODTs (8)

A. Freeze drying/ Lyophilization

B. Moulding

C. Sublimation

D. Spray drying

E. Direct compassion

F. Mass extrusion

G. Nanonization

H. Cotton candy process

I. Fast dissolving films

1) Freeze drying/Lyophilization [8]

It is the one of the first-generation techniques for preparing ODT, in which sublimation of water takes place from the product after freezing. The formulations show enhanced dissolution characteristics due to the appearance of glossy amorphous structure to bulking agents and sometimes to drug. The ideal drug characteristics for this process are relative water insolubility with fine particle size and good aqueous stability in suspension. Primary problems associated with water soluble drug are formation of eutectic mixture, because of freezing, which might collapse on sublimation. The addition of mannitol or crystal forming material induces crystallinity and imparts rigidly to amorphous material. The advantage of using freeze-drying process is that pharmaceutical substance can be processed at non elevated temperature thereby eliminated adverse thermal effects. High cost of equipment and processing limits the use of the process. Other disadvantages include lack of resistance necessary for standard blister packs of the final dosage forms.

2) Moulding [8]

These are two types of moulding process i.e., solvent method. Solvent method and heat method. Solvent method involves moistening the powder blend with a hydro-alcoholic solvent followed by compression at low pressure in moulded plates to form a wetted mass (compression moulding). Air-drying is done to remove the solvent. The tablet manufactured so formed is less compact than compressed tablets and possess a porous structure that hastens dissolution. In the heat moulding process a suspension is prepared that contains a drug, agar and sugar (e.g., mannitol or lactose). This suspension is poured in the blister packing wells, and then agar is solidified at the room temperature to form a jelly and dried at 30 under vacuum. The main concern about this moulded tablet is their mechanical strength, which can be achieved by using blinding agents. The spray congealing if a molten mixture of

hydrogenated cottonseed oil, sodium carbonate, lecithin, polyethylene glycol and an active ingredient into lactose-basedtablet masked drug particles. As compared to the Lyophilization technique, tablets produced by the moulding technique are easier to scale up for industrial scale manufacturing.

3) Sublimation [8]

This process involves addition of some inert volatile substance like urea, urethane, naphthalene, camphor, to other excipients and the compression of blend into tablet. Removal of volatile material by sublimation creates pores in tablet structure, due to which tablet dissolves when comes in contact with saliva. Additionally, several solvents like cyclohexane, benzene can also be used as pore forming agents. Mouth dissolving tablets with highly porous structure and good mechanical strength have been developed by this method.

4) Sprays-Drying [8]

Spray-drying for the production of MDTs. The formulation contained hydrolysed and non-hydrolysed gelatin as a bulking agents and sodium starch glycolate or croscarmellose as a disintegrate. By adding an acid (e.g., citric acid) or an alkali (e.g., sodium bicarbonate) disintegration and dissolution were further enhanced. The porous powder was obtained by spray drying the porous powder was obtained by spray drying the above suspension which was compressed into tablets. Tablets manufacturing by this method shows disintegration time < 20 sec in an aqueous medium.

5) Direct compression [8]

Direct compression represents the simplest and most cost-effective tablet manufacturing techniques. MDT can be prepared by using these techniques because of the availability of improved excipients especially super-disintegrates and sugar-based excipients.

(a)Super-disintegrates

(b)Sugar based excipients

6) Mass extrusion [8]

This technology involves softening of the active blend using the solvent mixture of water-soluble polyethylene glycol and methanol. This softened mass is extruded through the extruder or syringe and a cylindrical shaped extrude is obtain which are finally cut into even

segments using heated blade to form tablets. Granules of bitter drugs can be using this method to mask their taste.

7) Nanonization [8]

A recently developed Nano melt technology involves reduction in the particles size of drugs to nano size by wet-milling technique. Surface absorption of the nano crystals of the drugs is done on selected stabilizers for stabilizing them against agglomeration, which are then incorporated into the MDTs. The technique is mainly advantageous for poor water-soluble drugs and also for wide range of doses (up to 200mg of drug per unit).

8) Cotton candy process [8]

The FLASHDOSE is a MDDDS manufactured using shear form technology in an association with Ceform TI technology to eliminate the bitter taste of the medicaments [A matrix known as floss, with a combination of excipients, either alone or with drugs is prepared by using shear from technology. Like cotton-candy fibre floss is fibrous material made of saccharide such as a sucrose, dextrose, lactose and fructose temperatures ranging between 180-266 F. however other polysaccharides such as polymaltodextrin and poly-dextrose can be transformed into fibres at 30-40% lower temperature than sucrose. Due to this modification thermo labile drugs can be safely incorporate.

EVALUATION OF ORAL FAST DISINTEGRATING TABLET

A) PRE-FORMULATION STUDIES

1) Bulk density: Bulk density was determined by pouring the 5gm of powder in to a 100ml graduated cylinder. Then bulk volume (v) was noted. Bulk density was noted by using following formula

$$\text{Bulk density} = m/vb$$

m= mass of the powder

vb= bulk volume of the powder [9]

2) Tapped density: The measuring cylinder containing measured amount of the powder was tapped for specified number of tapping and time. The volume occupied by the powder after tapping and mass was noted.

Tapped density = m/vt

m = mass of the powder

vt = tapped volume of the powder [10]

3) Carr's index (or) percentage (%) compressibility: It indicates powder flow properties. It is expressed in percentage and it is given as

I= Tapped density – bulk density/ Tapped density x 100

Relationship between % compressibility and flowability [8]

% Compressibility	**Flow ability**
5 – 12	Excellent
12 – 16	Good
18 – 21	Fair passable
23 – 35	Poor
33 – 38	Very poor
<40	Very very poor

4) Hausner ratio: Indirect index of powder flow can be determined from Hausner ratio calculation [9]

Hausner ratio = Dt/Db

Dt = Tapped density

Db = Bulk density

Hausner ratio	**Flow property**
1.18	Excellent
1.19	Good
1.25	Passable
1.3 – 1.5	Very poor
>1.5	Very very poor

5) Angle of repose: It was calculated by using funnel method powder blend was poured on vertically placed funnel until cone of maximum height was formed

$$\mathbf{Tan\ \theta = h/r}$$

θ = Angle of repose

h = height of cone

r = radius of the cone base [8]

Angle of repose	**Type of flow**
<20	Excellent
20 – 30	Good
30 – 34	Passable
>34	Very poor

6) Porosity: Percent relative porosity was obtained using the relationship between apparent density and true density which is calculated by following formula

$$\varepsilon = (1 - \text{apparent density / true density}) \times 100$$ [13]

7) Voide volume: It was obtained by difference between bulk volume (Vb) and tapped volume (Vb). Voide volume can be calculated by following formula

$$V = Vb - Vp$$

Where,

Vb= bulk volume

Vp= tapped volume [12]

B) PRE-FORMULATION STUDIES

1) Tablet thickness: The thickness was measured by placing tablet between two arms of the vernier calipers.5 tablets were taken and their thickness was measured. [15]

2) Tablet hardness: The tablet hardness which is the force required to break a tablet in a diametric compression force. The hardness tester used in the study was Monsanto hardness tester. Which applies forces to the tablet diametrically with the help of an inbuilt spring. [12]

3) Weight variation test: Weight variation test was done by weighing 20 tablets individually by using

Calculating the average weight and comparing the individual tablet weight to the average weight. [8]

Average weight of tablet	% Deviation
80mg or less	± 10
More than 80mg but less than 250mg	± 7.5
250mg or more	± 5

4) Friability: Friability of the tablets was calculated by using Roche Friabilator (pharma test Germany). Twenty tablets were weighed on electronic weighing balance (Shimadzu Japan) and their weight was noted. Tablets were placed in the Friabilator. The Friabilator was operated at a speed of 25rpm for 4 minutes. After 4 minutes tablets were removed, dedusted and again weighed in order to determine final weight of the tablet.

$$\text{Friability (f)} = (1 - w_o/w) \times 100$$

W_o = weight of tablet before the test

W = weight of tablet after the test [9]

5) Wetting time: A glass petri dish was practically filled with water and a tablet was placed on the surface of a band of filter paper supported on a glass slide. The uptake of water occurred from the lower surface of the tablet. The time required for water to reach the center of the upper surface of the tablet was noted as wetting time. [10]

6) Water absorption ration: A piece of tissue paper folded twice was placed in a small petri dish containing 6ml of the water. A tablet was put on the paper of the time required for complete wetting was measured. The wetted tablet was then weighed. Water absorption ratio (R) was determined using following equation:

$$R = 10\ (w_a/w_b)$$

Where, W_b = weight of tablet before water absorption

$W_{a=}$ weight of tablet after water absorption [11]

7) Dispersion time: 10ml of water filled in the petri dish and put down the tablet at the center of the petri dish and note down the complete disintegration tablet. (18)

8) Drug content: Five tablets from each batch are weighed and powdered, 10mg equivalent of the powder is taken and diluted with 10ml of distilled water and the volume is made upto 100ml. From this 10ml of the solution is taken and the volume is made up to 100ml with distilled water. The absorbance of the solution is measured using UV-spectrophotometer at 271nm. (17)

9) Disintegration time: The disintegration test is performed using an USP disintegration apparatus with distilled water at 37 ± 0.5^0C. The time reported to obtain complete disintegration of 6 tablets are recorded and average is reported. (14)

10) Dissolution studies: The release rate of the formulated tablets is characterized using USP type 2 (paddle) at 50rpm 900ml of distilled water is used as dissolution medium. 10ml of blank media. The sample are withdrawn at 5, 10, 15, 30 and 45min. then analyzed using UV-spectrophotometry. (16)

CONCLUSION

In recent days, oral disintegrating tablets have gained more importance when compared to the conventional dosage forms due to their varied advantages. FDTs are the type of dosage forms that can disintegrate within 60 sec without the need for water. They have many advantages like rapid absorption with increased bioavailability, improved efficiency of the drugs. It can also be administered for patients who are bedridden, pediatric, and geriatrics. The key principle of FDT is to have faster disintegration, dissolution. This can be achieved by adding superdisintegrants or producing a porous structured tablet matrix. There are different methods to formulate FDTs like freeze drying technique, direct compression, sublimation method, etc. Though they have pronounced advantages, they have minimal disadvantages like poor mechanical strength, they are hygroscopic. Apart from having disadvantages, they are used widely due to their better patient's compliance. Due to the high market potentials, many drugs can be formulated as FDTs.

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