MOUTH DISSOLVING TABLET: SUPERLATIVE CONCLUSIVE DOSAGE IN SOLID FORM FOR MODERN AGE

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ABSTRACT
Regardless of different advancement in drug delivery system, oral route remains the perfect route for the administration of the any therapeutic agents because of the low cost of therapy, ease of administration, self medication, and patient compliance. MDTs have received a great demand during the last decade because MDTs are dissolving rapidly in saliva without need of water, overcome the problem of Dysphasia i.e difficulty in swallowing and provides quick onset of action. Some tablets are designed to dissolve very fast within a few seconds are known as true FDTs. Fast or Mouth dissolving tablets are basically formulated for pediatric, geriatric, and bedridden patients and for active patients who are busy and travelling and may not have access to the water. In this review article, various conventional technologies like Freeze drying, Tablet Molding, Spray Drying, direct compression and patented technologies like Zydis, Orasolv, Durasolv, Flashtab, WOW Tab, Pharmaburst etc are described to formulate MDTs. Moreover, various excipients used to formulate MDTs, how to develop the taste for the drugs having bitter taste, and how to conduct characterization and evaluations of MDTs are also described.

Keywords: Dosage form for modern age, Oral Drug delivery system, Mouth dissolving Tablet (MDTs), Patented Technologies.

INTRODUCTION
Regardless of different advancements in drug delivery system, oral route remains the perfect route for the administration of the therapeutic agents because of low cost of therapy, ease of administration, accurate dosage, self medication, pain avoidance and most importantly the patient compliance [1].

Many Pharmaceutical dosages are administered in the form of pills, granules, powders, and liquids. Generally, a pill id design for swallowing intact or chewing to deliver a precise amount of medication to the patients. The pills which include tablets and capsules are able to retain their shape under the moderate pressure. However, in some
patients particularly pediatric and geriatric patients may suffer from Dysphasia (Difficulty in swallowing) [2, 3]. However, in case of dysphasia of geriatric patients, the underdeveloped muscular and nervous system in young individuals and incase of uncooperative patients many problems may occur but Dysphasia is common phenomenon which leads to poor patient compliance.

According to study people having Dysphasia problems are about 35% in the general population, and additional 30-40% of elderly institutionalized patients as well as 18-22% of all the persons in long term care facilities. Another study shows that an estimated 50% of population was suffered from this problem [4]. Traditional tablet and capsules are administered with 8 –oz. glass of water may be inconvenient or impractical for some patients. For example, very elderly patients may not be able to swallow a daily dose of Anti-depressant. A schizophrenic patient can hide a conventional tablet under his or her tongue to avoid their daily dose of Antipsychotic. A middle-aged women undergoing radiation therapy for breast cancer may be too nauseous to swallow her H2-blocker [5, 6].

These studies shows that urgent need of a new dosage form which will be an effective therapy and can improve patient compliance. As the cost and risk for developing a new chemical entity are becoming higher every year, development of new drug delivery system for existing drug may be alternate strategies for many Pharmaceutical industries [7].

New drug delivery systems are aimed at improving efficacy and bioavailability of existing drugs, and as well as providing benefits of reduced dosing frequency, minimizing side effects and enhanced patient compliance. Mouth dissolving tablets are a perfect fit for all of these patients. Solid dosage form that can be dissolved in or suspended with saliva in mouth and result in easy swallowing have a huge marketing potential among the pediatric and geriatric population, as well as other patients who prefer the convenience of easily administered dosage forms [7].

The MDT technology, which makes tablets dissolve or disintegrate in the mouth without additional water intake. The MDT formulation is defined by the Food and Drug Administration (FDA) as “A solid dosage form containing medical substances which disintegrates rapidly, usually within a seconds, when placed upon the tongue.” According
European Pharmacopoeia, “the MDT should disperse/disintegrate in less than three minutes. Mouth dissolving tablets are also called as fast-dissolving tablets, melt-in mouth tablets, Orodispersible tablets, rapimelts, porous tablets, quick dissolving etc. The basic approach in development of MDT is the use of superdisintegrants, which provide instantaneous disintegration of tablet after putting on tongue, their by release the drug in saliva. The mouth dissolving tablets are rapidly dissolved or disintegrate by the use of superdisintegrants \cite{8,9}.

**Mechanism:**

Bioavailability of a drug depends on absorption of the drug, which is affected by solubility of the drug in gastrointestinal fluid and permeability of the drug across gastrointestinal membrane. The solubility of a drug mainly depends on physiochemical properties of the drug. The rate of drug dissolution is greatly influenced by disintegration of the tablet.

Disintegrants are important excipient of the tablet formulation, they are always added to tablet to induce breakup of tablet when they come in contact with aqueous fluid and this process of desegregation of constituent particles before the drug dissolution occurs, is known as disintegration process and excipients which induce this process are known as disintegrants. The objectives behind addition of disintegrants are to increase surface area of the tablet fragments and to overcome cohesive forces that keep particles together.

**Ideal Properties of MDTs** \cite{10}:

An ideal MDT should:

- Require no water for oral administration.
- Have a pleasing mouth feel.
- Have an acceptable taste masking property.
- Leave minimal or no residue in mouth after administration.
- Exhibit low sensitivity to environment.
condition. (Temperature & Humidity)

- Adaptable and amenable using conventional processing and packaging equipment at low cost.

**Advantages**[^11]:

- Administration to the patient who cannot swallow such as elderly, bedridden patients, patients affected by renal failure & patients who refuse to swallow such as pediatric, geriatric and psychiatric patients.
- Rapid drug therapy intervention.
- Achieve increased bioavailability /rapid absorption though pre-gastric absorption of drugs from mouth, pharynx and esophagus as saliva passes down.
- Ease of administration.
- Good mouth feel property helps to change the perception of medication as bitter pill particularly for pediatric patients.
- Risk of choking and suffocation during oral administration of conventional formulation due to physical obstruction is avoided, thus providing improved safety.
- New business opportunity like product differentiation.

**Disadvantages**[^12]:

- Mouth dissolving tablet is Hygroscopic in nature so must keep in dry place.
- Mouth dissolving tablet requires special packaging for properly stabilization & safety of the stable product.
- The tablets may leave unpleasant taste in case if it is not formulated properly.

1. **TECHNIQUES FOR PREPARING MDTS:**

Various techniques have been reported for the formulation of MDTs. They are summarized as follows.
# TECHNOLOGIES

## (A) CONVENTIONAL TECHNOLOGIES

1. **Freeze-Drying**
   - **Detail:** It is a process in which water is sublimed from the product after it is frozen. It creates an amorphous porous structure that can dissolve rapidly.
   - **Advantage:** Improved dissolution, absorption and increase in bioavailability.
   - **Disadvantage:** Expensive and time consuming technique. Poor Packaging and stability issues.

2. **Tablet Molding**
   - **Detail:** Tablet produced by moulding are solid dispersion. There is of two types i.e., solvent method and heat method. Solvent method involves moistening the powder blend with a hydro alcoholic solvent followed by compression at low pressures in molded plates to form a wetted mass (compression molding). The solvent is then removed by air-drying. The heat molding process involves
   - **Advantage:** Easier to scale up for industrial manufacture.
   - **Disadvantage:** Taste masking is an added problem to this technology.

## (B) PATENTED TECHNOLOGIES

1. **ZYDISTECHNOLOGY**
2. **ORASOLV TECHNOLOGY**
3. **DURASOLV TECHNOLOGY**
4. **FLASH DOSE TECHNOLOGY**
5. **WOWTAB TECHNOLOGY**
6. **FLASH TAB TECHNOLOGY**
7. **FROSTA TECHNOLOGY**
preparation of a suspension that contains a drug, agar and sugar (e.g. mannitol or lactose) and pouring the suspension in the blister packaging wells, solidifying the agar at the room temperature to form a jelly and drying at 30°C under vacuum.

Spray drying is process by which highly porous, fine powders can be produced. Tablets were prepared by using Gelatin as a supporting agent and as a matrix, Mannitol as a bulking agent and sodium starch glycolate or crosscarmelllose or crospovidone are used as superdisintegrants. Disintegration and dissolution was further enhanced by using citric acid or sodium bicarbonate.

To generate a porous matrix, volatile ingredients are incorporated in the formulation that is later subjected to a process of sublimation. Highly volatile ingredients like ammonium bicarbonate, ammonium carbonate, benzoic acid, camphor, naphthalene, urea, urethane and phthalic anhydride may be compressed along with other excipients into a tablet. This volatile material is then removed by sublimation leaving behind a highly porous matrix. Even solvents like cyclohexane; benzene can be used as pore forming agents.

### B. PATENTED TECHNOLOGIES [13-23].

<table>
<thead>
<tr>
<th>Name of Patented Technology</th>
<th>Method of Preparation</th>
<th>Materials Used</th>
<th>Advantages</th>
<th>Limitations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Zydis Technology (R.P.Schere)</td>
<td>Freeze drying (Lyophilization)</td>
<td>Polymer – gives strength &amp; rigidity,</td>
<td>• When zydis units are put into mouth, it</td>
<td>• The amount of the drug that can be incorporated is less than 400 mg for</td>
</tr>
</tbody>
</table>
| Corporation | Polysaccharides – To impart crystalinity & hardness to the matrix & improve palatability, Collapse protectant – To prevent the product from shrinking in its packaging. | disintegrates quickly (<3seconds) & not required water for swallowing | insoluble & 60 mg for soluble drugs.  
• The Particle size of the insoluble drugs should be between 50 to 200 μm.
|---|---|---|
| Orasolv & Duroslov Technology (Cima Labs) [14-16] | Direct Compression | Effervescent disintegration Pairs (acid + Carbonate Source) in a concentration of 20 – 25% of the total weight of tablet is used, Non-direct & direct compressible fillers & lubricants (Particle Size between between 20 to 65 μm & 85% of the particles >100 μm in size respectively) | • As compare to the conventional tablet formulation, higher amount of hydrophobic lubricants like magnesium stearate (1 – 2.5%) can be used instead of 0.2 – 1%.  
• The lubricant blending time can also be increased to 10 – 25 minutes.  
• Low compression force is required.  
• Due to the soft & fragile nature of the tablets, a special packaging system i.e Paksolv ("dome shaped" blister package that prevents the vertical movement of the tablets within the depressions) was developed to protect the tablets from breaking during transport and storage (Wehling et al., 1993).
| WOW Tab Technology (Mizumoto & Masuda) [15-18] | Wet granulation | Low moldability polysaccharides (lactose, mannitol, glucose, sucrose & Xylitol) are used as main component, high moldability polysaccharides (maltos, maltitol, & sorbitol) etc. | • WOW means without water. So, no need of water during swallowing.  
• Only combination of low moldability & high moldability polysaccharides can give desired properties of MDTs because low moldability polysaccharides give hardness between 0 – 2 kg while high moldability polysaccharides give hardness > 2 kg. |
<table>
<thead>
<tr>
<th>Technology</th>
<th>Method</th>
<th>Ingredients</th>
<th>Properties</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Flash Tab Technology (Cousin et al., 1995)</td>
<td>Dry or Wet Granulation</td>
<td>Drug, diluents, binder, disintegrants, swelling agents etc.</td>
<td>• Disintegrate in mouth within 1 minute.</td>
<td>-</td>
</tr>
</tbody>
</table>
| Adva Tab [19-21]                               | Wet granulation (but in this method, lubricant is sprayed on each tablet during production) | Drug, diluents, binder, disintegrants, and lubricants etc.                   | • Adva Tab produces the tablets with 10 – 30 times less hydrophobic lubricant & 30% stronger as compared to the conventional tablets.  
• Higher concentration of drugs & coated drug particles can be used.  
• As the tablets produced by this technique are hard, it does not required special packaging. | -                         |
| Pharmaburst Technology [21,22]                 | Wet Granulation or Direct Compression (Compress is carried out under normal humidity & Temperature) | Drug, Flavor, Lubricant, & Co-processed excipients (can be used 50 – 80% depending upon desired characteristics) | • Drug loading – up to 700 mg.  
• Tablet dissolves within 30 - 40 seconds. | -                         |
| Quick – Dis Technology (Lavipharm) [22,23]     | Quick dissolving film                                                 | -                                                                          | • When this film comes in contact with water, it dissolves within 5–10 seconds. | -                         |
C. COMMERCIAL PRODUCTS [21-23]:-

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Active Ingredient</th>
<th>Application</th>
<th>Company</th>
</tr>
</thead>
<tbody>
<tr>
<td>Claritin® Redi Tab®</td>
<td>Loratidine</td>
<td>Antihistamine</td>
<td>Scherig Corporation</td>
</tr>
<tr>
<td>Pepeid® ODT</td>
<td>Femotedene</td>
<td>Antiulcer</td>
<td>Merck</td>
</tr>
<tr>
<td>Feldene Melt®</td>
<td>Piroxicam</td>
<td>NSAIDs</td>
<td>Pfizer</td>
</tr>
<tr>
<td>Zyperxa®</td>
<td>Olazepine</td>
<td>Psychotropic</td>
<td>Eli Lilly</td>
</tr>
<tr>
<td>Maxalt® - MLT®</td>
<td>Rzatriptan Benzoate</td>
<td>Migrain</td>
<td>Merck</td>
</tr>
<tr>
<td>Zofran® ODT</td>
<td>Ondansentron</td>
<td>Anti-emetic</td>
<td>Glaxo Smith Kline</td>
</tr>
<tr>
<td>Zelapar™</td>
<td>Selegiline</td>
<td>Parkinsons disease</td>
<td>Elanl Amarin Corporation</td>
</tr>
<tr>
<td>Klonopin® Wafer</td>
<td>Clonazepam</td>
<td>Sedation</td>
<td>Roche</td>
</tr>
<tr>
<td>Childrens Dimetapp</td>
<td>Loratidine</td>
<td>Allergy</td>
<td>Wyeth Consumer Health care</td>
</tr>
<tr>
<td>Propulsid® Quicksolv®</td>
<td>Cisapride Monohydrae</td>
<td>Gastrointestinal Prokinetic Agent</td>
<td>Jannsen</td>
</tr>
<tr>
<td>Imodium Insatant Melt</td>
<td>Loperamide HCL</td>
<td>Antidiarrheal</td>
<td>Jannsen</td>
</tr>
<tr>
<td>Tempra Quicksolv®</td>
<td>Acetamenofen</td>
<td>Analgesic</td>
<td>Bristol-Mters Squibb</td>
</tr>
<tr>
<td>Remeron® Soltab®</td>
<td>Mirtazapine</td>
<td>Anti-Depression</td>
<td>Organon Inc.</td>
</tr>
<tr>
<td>Benadryl® Fastmelt®</td>
<td>Diphenhydramine Citrate</td>
<td>Sinus Pressure Relief</td>
<td>Pfizer</td>
</tr>
<tr>
<td>Nulev®</td>
<td>Hyocynine Sulfate</td>
<td>Antiulcer</td>
<td>Schwarz Pharma</td>
</tr>
<tr>
<td>Nasea OD</td>
<td>Ramosetoron HCL</td>
<td>Antiemetic</td>
<td>Yamanouchi</td>
</tr>
</tbody>
</table>

2. EXCIPIENTS USED IN THE FORMULATION OF MDTs [23-27]:-

<table>
<thead>
<tr>
<th>Category of Excipients</th>
<th>Concentration of excipients in which they are added in the formulation</th>
<th>Characteristics</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bulking Agents</td>
<td>10 to 90% of the total</td>
<td>Generally they are added to</td>
<td>Incase of MDTs, sugar based bulking agents are used</td>
</tr>
<tr>
<td>Emulsifying Agents</td>
<td>0.05 to 15% by weight of the final formulation.</td>
<td></td>
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<tr>
<td>---------------------</td>
<td>-------------------------------------------------</td>
<td></td>
<td></td>
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<tr>
<td></td>
<td>It imparts rapid disintegration &amp; drug release without chewing, swallowing &amp; drinking water.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>It stabilize the immiscible blends &amp; enhancing bioavailability.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Alkyl sulphates, Propylene Glycol Esters, lecithin, and Sucrose.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Super disintegrants</td>
<td>Effective at lower concentration.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Higher disintegration capacity &amp; Mechanical strength.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>It acts by four mechanisms: Swelling, Wicking, Deformation, and Particle/Particle Repulsive forces.</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cross linked cellulose, Cross linked PVP, Cross linked Starch, Cross linked alginic acid, Soy Polysaccharides, Calcium Silicate etc.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lubricants</td>
<td>1-2%</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>To remove grittiness &amp; assist in drug transport mechanism from mouth down to</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>Magnesium Stearate, Talc, Sodium Stearyl Fumarate etc.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Flavors</td>
<td>According to the taste of the drug</td>
<td>To mask the bitter taste of the drug &amp; make the product more acceptable to the patients.</td>
<td>Natural as well as synthetic flavors are used. E.g: Dextrose, Fructose, aspartame, Sodium Saccharine, and Sucralose etc.</td>
</tr>
<tr>
<td>-------------------------</td>
<td>------------------------------------------------------------------------------------------------------</td>
<td>----------------------------------------------------------------------------------------</td>
<td>-----------------------------------------------------------------------------------------------------------------</td>
</tr>
</tbody>
</table>

- **Selection of Flavors:**

  Flavor selection was done by subjective evaluation by a panel of taste sensitive individuals as shown in the Taste Protocol. These in-vivo evaluations consist of double blind cross-over study, carried out on a trained taste panel of healthy volunteers with the sound organoleptic senses, with their prior consent. On placing the dosage form in the oral cavity, disintegration time was noted after which it was further held in mouth for 60 seconds by each volunteer, and taste was recorded using numerical scale against the pure drug (Control). After 60 seconds, disintegrated tablet was spitted out and mouth was rinsed thoroughly with mineral water. The numerical scale bears 0-tasteless, 1-Slight, 2-Slight to Moderate, 3-Moderate, 4-Moderate to Strong, 5-Strong. The taste protocol for selection of flavors is given below.

**TASTE PROTOCOL**

**INFORMED CONSENT FORM FOR TASTE OPTIMIZATION STUDY**

This informed consent form is for inviting to participate in “Taste Optimization study” for Research project which includes taste optimization by using different flavors.

[Name of Principle Investigator]:
[Name of Organization]:
[Name of Project and Version]:
This Informed Consent Form has two parts:
PART I: Information Sheet (to share information about the research with you)
PART II: Certificate of Consent (for signatures if you agree to take part)

Type of Research Intervention

This study will involve your participation in taste Optimization study.

Participant selection

You are being invited to take part in this study because I feel that your experience as a healthcare professional can contribute much more to our understanding. And as a very keen observer, you can answer (score) the questions (quality) in a very precise manner as compared to others, for the questionnaire pertaining to product assessment.

Voluntary Participation

Your participation in this study is voluntary. It is your choice whether to participate or not. You may change your mind later and stop participating even if you agreed earlier.

Procedures and Protocol

A. Unfamiliar Procedures

1) Involving randomization or blinding. The participants will be randomised into 3 group test group (MDT with taste masked drug), positive control (MDT with drug), negative control (MDT without drug-placebo) and so they have two in three chances of getting the test drug. This will be a single blind study; means only evaluator knows which participant consume which product.

2) Involving an inactive drug or placebo

A placebo looks like real medicine but it is not. It is a dummy or pretend medicine. It has no effect on a person because it has no real medicine in it.

Description of the Procedure

You have to disperse the MDT product for predetermined time of 60 secs without swallowing & afterwards you have to give residual sample to researcher. You have been provided a score card for giving score to different qualities of the MDT product that you feel during dispersion. Note: This procedure does not require any blood sample collection.

Benefits
There will be no direct benefit to you, but your participation is likely to help us to find out marketing potential for business opportunity of formulated MDT product.

Confidentiality & Sharing the Results

I will not be sharing the identity of those participating in the research with anyone. The information that we collect from this research project will be kept confidential & not be identified by your name but by a number. The knowledge that we get from doing this study will be shared with you before it is made widely available to the public.

Right to Refuse or Withdraw

You do not have to take part in this research if you do not wish to do so. You may also stop participating in the study at any time you choose; all of your rights will still be respected.

B) For Researcher

I have accurately read or witnessed the accurate reading of the consent form to the potential participant, and the individual has had the opportunity to ask questions. I confirm that the individual has given consent freely.

A copy of this Informed Consent Form has been provided to participants by the researcher.

Name of Researcher ___________________________

Signature of Researcher _________________________

GROUP CODE: A / B / C / D / E

PARTICIPANT CODE:__________

PRODUCT CODE___________

A) PRODUCT TASTE (SWEET OR BITTER)
A) PRODUCT DISPERSION TIME (IN MINUTES)

INITIALS FOR NAME OF THE PARTICIPANT:  NAME OF THE RESEARCHER:
SIGNATURE OF THE PARTICIPANT:  SIGNATURE OF THE RESEARCHER:
DATE:  DATE:

4. CHARACTERIZATION & EVALUATION OF MDTs:  
1) Measurement of Tablet Tensile Strength or Hardness:

The tablet tensile strength is the force required to break the tablet in the diametric compression force using a tablet hardness tester. For measuring the hardness of the tablets, the plunger of the hardness tester is driven down at a speed of 20 mm/min. Tensile strength (T) for crushing the tablet is calculated using the following equation.

\[ T = \frac{2F}{\pi dt} \]

Where, F is the crushing load, and d and t denote the diameter and thickness of the tablet, respectively.

Though this is widely accepted method to determine tablet tensile strength, it is not applicable to the tablets which are prepared by lyophilization technique (freeze dried process) & Flash Dose Tablets prepared by cotton candy process. This test is best for the tablets prepared by direct compression and molding methods.

II) Friability:

The pharmacopoieal limit for the test of friability for a tablet is not greater than 1% using tablet friability apparatus. This test is carried out at 25 rpm for 4 minutes (100 rotations). However, it becomes a challenge for a formulator to achieve friability below 1% for MDTs by keeping hardness as low as possible to achieve minimum disintegration time. This test is again not suitable for the tablets prepared by lyophilization technique and
Flash Dose Tablets, but it is good for tablets prepared by direct compression & molding techniques.

III) Moisture uptake Study $^{[32, 33]}$:

MDTs contain high amount of hydrophilic excipients with minimum hardness which together contribute to their increased susceptibility to moisture uptake. In order to maintain their physical appearance and surface morphology, special attention is required during the storage and packaging of MDTs. Therefore, moisture uptake study is strongly recommended for MDTs. The test can be carried out by keeping ten tablets along with calcium chloride in a dessicator maintained at 37°C for 24 hrs to ensure complete drying of the tablets. The tablets are then weighed and exposed to the 75%RH, at room temperature for 2 weeks. The required humidity can be achieved by using saturated sodium chloride solution in a dessicator for 24 hrs. the tablets are reweighed and % increase in weight is recorded. If moisture uptake tendency is high then it requires dehumidified area during manufacturing and packaging.

IV) Wetting Time and Absorption Ratio $^{[34-36]}$:

A study on wetting time and water absorption ratio reported the use of a piece of double folded tissue paper placed in a petridish containing 6ml of water. One tablet was placed on this paper and the time for complete wetting of the tablet was noted as wetting time. The wetted tablet was then weighed and the water absorption ratio, R, was determined according to the following equation.

$$R = 100(W_a - W_b) / W_b$$

Where $W_b$ and $W_a$ are the weights of tablet before and after water absorption, respectively.

V) Measurement of Tablet Porosity $^{[35]}$:

To measure the tablet porosity which is a relative assessment of the degree of water penetration in the formulation, the mercury penetration porisometer can be used. This instrument works on the basis of capillary rise phenomenon where excess liquid is required to cause anon wetting liquid to climb up a narrow capillary. The pressure difference across the interface is calculated by Washburn equation II, where pressure drop is inversely related to poresize.

$$\Delta P = -(2\gamma/r) \cos \theta$$
Where, $\gamma$ = Surface tension of the liquid
$r$ = Perpendicular radius
$\theta$ = Angle of contact between the liquid & capillary walls

VI) Fineness of Dispersion \cite{36-38}:

This test is specified by EP for MDTs. It is an assessment of grittiness which occurs due to the disintegration of the tablets into the smaller particles. This test is carried out by placing 2 tablets in 100 ml of water and stirs it till the tablets get disintegrated. If the complete dispersion passes through a sieve screen with a nominal mesh aperture of 710 µm without leaving any residue on the screen them the formulation is considered as a smooth dispersion.

VII) In Vivo Determination of Disintegration Time \cite{39-41}:

In vivo disintegration tests of MDTs can be conducted on individual subjects. Subjects are usually randomized to receive the treatments and then directed to clean their mouths with water. Tablets are placed on their tongues, and the time for the disintegration is measured by immediately starting a stopwatch. The volunteers are allowed to move MDTs against the upper roof of the mouth with their tongue and to cause gentle tumbling action on the tablet without biting on it. Immediately after the last noticeable granule has disintegrated, the stopwatch is stopped and the time is recorded.

However, the results from this type of test typically reveal unsatisfactory reproducibility and are not reliable as the difference in the disintegration time is few seconds in most cases. In addition, the in vivo disintegration test has its own limitation of issues related to ethics and safety of the volunteers. EP has set the limit of 3 mins for disintegration time of MDTs using conventional disintegration apparatus. However, no special apparatus is mentioned in the pharmacopoeias for disintegration test of MDTs and conventional method available seems to be inappropriate for MDTs. This is because of the extreme operating conditions in the disintegration apparatus which fails to provide a significant discrimination among the rapidly disintegration tablets. Furthermore, the conventional test employs a relatively huge volume of test solution (900 ml) compared to the volume of saliva in human buccal cavity, which is less than 6ml. Therefore, the results obtained from the conventional disintegration test do not reflect the actual disintegration rate in the...
human mouth which usually ranges from 5-30 secs. To overcome these issues, several new methods have been proposed, which are as follows.

VII) In Vitro Determination of Disintegration Time\cite{41-45}:

a) **Modified U.S. Pharmacopeia Method:**

Instead of using the disintegration apparatus mentioned in the U.S. P, a modified method has been proposed. The disintegration apparatus was the same as the USP dissolution apparatus type 2, which uses a paddle stirring element and 1000 ml cylindrical vessel at 37°C. Distilled water was used as a disintegration medium (900ml), instead of a buffer solution. A tablet to be tested was put on the bottom of a sinker, which was placed in the middle of a vessel and hung by hook with a distance of 6 to 8.5 cm. Disintegration time was measured at the point at which the tablet disintegrated and passed through the screen of the sinker completely. The size of the mesh of the sinker was 3-3.5 mm in height and 3.5-4 mm in width.

![Fig 1.5: Schematic View Of Modified Dissolution Apparatus For Disintegration Test](image)

b) **Disintegration Test Using Texture Analyzer:**

A texture analyzer was used to measure the start and end time points of tablet disintegration. On the tablets, a constant penetration force is applied via cylindrical flat-ended prob. The tablet is immersed in a defined volume of distilled water under the constant force. The graph of time Vs distance is plotted which shows the probe travelled into the tablet. From the typical time-distance profiles, generated by the texture-analysis software, enabled the calculation of the starting and ending time of disintegration.
5. SUMMARY AND CONCLUSION:

MDTs can offer some advantages over conventional oral dosage form like improve patient compliance, provide a rapid onset of action, increase absorption and thereby increase bioavailability. MDTs need to be formulated particularly for pediatric, geriatric, bedridden, psychotic patient, and for the active persons who are busy in travelling & may not have access to the water. These types of products give opportunity for the product line extension in the market and extension of the innovator patent term. By considering the benefits of MDTs, now a day, Pharmaceutical companies try to develop majority of the oral formulations in mouth dissolving forms.

REFERENCES


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