1. Introduction

Oral route of drug administration for systemic delivery of therapeutic agents is widely accepted due to exact dosage, ignoble cost remedies, non incursive technique and comfort management prime to great extent of patient conformity, versatility with respect to type and dose of the drug, and suitability to scale up\textsuperscript{1,2}.

Despite all the advantages, conventional tablets generally do not prove useful in situations. The geriatric patients face difficult in swallowing of traditional tablets and capsules. The following factors make geriatric patients difficult in administration of solid dosage form:

- Physiological and neurological context altered as age increases
- Hand tremors
- Deterioration of eyesight
- Ability to hear
- Reminiscence
- Chances in throttling\textsuperscript{3}

Moreover, the patient suffering from severe nausea, paediatric, small children, cerebrally challenged and uncooperative patients faced problem in taking tablets and capsules. Due to improper development of muscular and nervous control, the pediatric get troubled while taking solid dosage form\textsuperscript{4-6}.

Following patient also get difficult in taking solid dosage from:

- During journey
- Prompt allergically attack
- Cold fever
Inaccessibility of drinking water

Patients wandering with sparse or no acquire to water

Various types of tablets available in the market:

- Compressed Tablets
- Buccal or Sublingual tablets
- Molded tablets or Tablet triturates
- Enteric Coated tablets
- Layered tablets
- Mouth dissolving tablets
- Film coated Tablets
- Multiple –coated tablets
- Press coated tablets
- Controlled release tablets
- Sugar –coated tablets
- Tablets for solution

Above problem can be overcome by using mouth dissolving tablet (MDT). The MDT within seconds get disintegrates, and release drug on putting tongue. The disintegrated drug easily disperses in saliva and passes down into stomach. The bioavailability of MDT is more as compared to conventional solid dosage from$^{7,8}$.

1.1 Mouth dissolving tablets

As per the Food and Drug Administration (FDA), MDT is tablet which disintegrates within seconds after putting upon the tongue. After disintegration of DT form gel like substances, and this facilitate the patients in easy
swallowing of drugs. The Pharmacopoeia mentioned that the disintegration time of MDT varies from a few seconds to more than a minute⁹-¹¹.

1.1.1 Ideal Properties of MDTs¹²,¹³

It should not need aqua for consuming. It should ideally in the mouth less than few seconds.

- Taste should be palatable.
- Should withstand handling and packing forces.
- Should leave pleasant after feel in mouth.
- Following administration of MDT it is supposed to not leave any residues of tablets in the mouth.
- It resists the humidity and temperature during transportation.

1.1.2 Advantages of MDTs¹⁴,¹⁵

MDTs tender coupled utilities of tablets or capsules and syrup dose forms along with highly valued characteristics.

1.1.3 Precise dosing: The MDT furnishes comfort and perfect substitute for geriatric and pediatric patients.

1.1.4 Improved bioavailability: The bioavailability of mouth dissolving tablets is improved because it directly absorb from the mouth, pharynx and esophagus.

1.1.5 Prompt action: The mouth dissolving tablets disintegrated promptly along with fast dissolution and incorporation in oral cavity, it causes rapid inception of therapeutic action.

1.1.6 Patient compliance: It is suitable doses for patients who are roaming and do not have an instant approach to water, because it does not required water to swallow the tablet.

1.1.7 Effortlessness administration: The patients who have painfulness in consuming tablets, for them it is useful to administer mouth dissolving tablets.
1.1.8 **Obstruction free:** The MDT is considered more safe dosage form because during administration of these tablets there is no risk of suffocation in airways.

1.1.9 **Improved palatability:** The taste masking substances are used to enhance the palatability of MDT particularly for pediatric patients.

1.1.10 **Easy packaging:** No special wrapping needed, and can be packed in push through blisters.

1.1.11 **Cost impressive:** The MDT are low cost due to traditional preparing and packaging equipment.

1.1.12 **Salient Features of MDTs**

- The paediatric and geriatric patients can easily administer the MDT.
- It produces accurate and perfect dosing as compared to liquids.
- It produces rapid onset of action due to quick dissolution of drug.
- It enhanced the bioavailability of drug.
Fig 1.1: Various routes of administration of oral dosage form

1.1.13 Disadvantage of MDTs

- MDT must place in dried place due to its hygroscopic characters.
- MDTs produces mouth feeling in some cases.
- To make MDT more stable it requires special packaging.

1.1.14 Potential Candidates

- NSAID’S,
- Anti-emetics,
- Anti-histaminics,
- Anti-migraine
- Anti-psychotic (Neuroleptics)
- Cardiovascular drugs
- Drugs for erectile dysfunction
1.1.15 Needs\textsuperscript{15,18}

The MDT are highly used by the sufferers who are unable to consume the tablets, so that its manufacturing process should be optimize to lower the cost of tablets.

1.2 Manufacturing and marketing factors

In the competition of era the pharmaceutical industrialist are more focusing towards such doses form which is easily acceptable by patient. The MDT considered more convenient to patient because it is easily administered\textsuperscript{18}. The physical properties of mouth dissolving tablets can be regulating by manufacturing practices.

1.3 Challenges in formulating mouth dissolving tablets\textsuperscript{19}

1.3.1 Palatability

Generally, tablets are unpleasant, usually MDT comprise the medicament in a taste-masked form. When MDT placed on the tongue, it rapidly disintegrates and the active ingredients approach towards the taste buds. Therefore, to mask unwanted taste of the active ingredients is very difficult for patient compliance.

1.3.2 Mechanical strength

The MDT is friable because they are prepared from highly porous and soft-molded matrices. But it is very obstinate about to manage tablets. Therefore for caring of MDT, it requires specialized peel-off blister packing. This packing of MDT can increase the cost. The MDT can make hard and stable by preparing with Wow tab and durasolv methods. This can permit the tablet to put in multi-dose bottles.

1.3.3 Hygroscopicity

Mostly MDT is hygroscopic nature, and it is very difficult to maintain the physical property under normal conditions of temperature and humidity.
However, it required specialized packaging for the protection of tablets; and this can increase the cost of products.

1.3.4 Amount of drug

The methods available for formulation MDT are very limited. The lyophilized dosage forms of tablet consisting smaller than 400 mg for unsolvable drugs and 60 mg for soluble active constituents. This property can make difficult to prepare MDT.

1.3.5 Aqueous solubility

The medicament and ingredient used in the preparation of MDT are generally water soluble. This water solubility property makes formulation very difficult to prepare. This problem can be overcome by utilizing matrix-forming dosage form.

1.3.6 Size of tablet

The size of tablet play important role in the administration of a tablet. As per scientific data it has been documented that the size of MDT should be 7-8 mm to swallow in better prospects. But it very difficult to handle the tablets size smaller to 8 mm.

1.4 Ingredients for mouth dissolving tablets\textsuperscript{20}

The ingredients used in preparing of MDT have such qualities to rapid liberation of the drug form tablets, following in quicker dissolution. this issue comprises together the medicaments and the inactive ingredients.

1.4.1 Drug

The concluding features of a medicament for decomposition in the mouth and pre gastric absorption from MDTs includes:

- No bitter taste
- Active ingredients are less than 20 mg
- Easily solubilize in saliva
Permeate to absorb in oral mucosal tissue

1.4.2 Excipients

Ingredients being an integral ingredient in formulation require understanding of the nature of inactive ingredients to impede interaction with the API. When these excipients are used in preparation of MDT, they confer the desired organoleptic characters and product effectiveness. The expense and character of excipients are therefore, significant in its preference.

1.4.3 Binders

The binders are used to binds the excipients and active ingredient in various doses forms. The proper selection of binders is essential in formulation of MDT because to maintain the physical property of tablets. The binders used in the MDT formulations are liquid or semi-solid or combinations of different molecular weights such as polyethylene glycol. The usually available binders are Acacia, Tragacanth, Starch paste, Cellulose (natural binders); HPMC, Hydroxy Propyl Cellulose, PVP, Polyethylene Glycol (PEG), Polymethacrylates, Polyvinyl Alcohols, (synthetic/semisynthetic polymer).
1.4.4 Bulking materials

The bulking material is used in the MDT in the form of diluent and filler. These substances can enhance the textural features which heighten the disintegration of MDT in the mouth. The sugar-based bulking agents endorsed in this does form. Among these the mannitol has intense aqueous solubility and pleasant sensory impression. The MDT consisting of 10-90% bulking agent by weight of the final composition of tablets.

1.4.5 Lubricants

Lubricants like aerosil, talc and magnesium stearate are not essential excipients but they remove the roughness property. This can also help in movement of drug from the oral cavity to the abdomen. The lubricants help in forming MDT more pleasant after dissolving in the mouth.

1.4.6 Flavours and sweeteners

Flavours and sweeteners prepare the products further edible and acceptable for patients. It facilitates in overwhelming unpleasantness and unacceptable tastes of excipients present in MDT. Flavor obtained from the synthetic and natural sources are used to enhance the organoleptic qualities of MDT. The sugar, dextrose and fructose are used as sweetener, and available in the market at vide range. The sugar alcohols, sucralose, sodium saccharin and aspartame are sweetener come under non-nutritive category.

1.4.7 Super disintegrates

Super disintegrates act as the main ingredient of MDTs which when added to a tablet it facilitate in the dissolution of the solid mass when it is placed into a saliva. They are productive in low concentration, compressibility and outpouring capacity is least effected. The various super disintegrate are Sodium starch glycolate, croscarmellose sodium, crospovidone and low substituted hydroxyl propyl cellulose.
Table 1.1: Different types of superdisintegrants

<table>
<thead>
<tr>
<th>Superdisintegrants</th>
<th>Example</th>
<th>Mechanism action</th>
<th>Of Special comment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Crosscarmellose® Ac-Di-Sol® Nyme ZSX® Primellose® Solutab® Vivasol® L-HPC</td>
<td>Crosslinked cellulose</td>
<td>- Swells 4-8 folds in &lt; 10 seconds. - Swelling and wicking both.</td>
<td>Swells in two dimensions. Direct compression or granulation Starch free</td>
</tr>
<tr>
<td>Crosspovidone Crosspovidon M® Kolliodon® Polyplasdone®</td>
<td>Crosslinked PVP</td>
<td>- Swells very little and returns to original size after compression but act by capillary action</td>
<td>Water insoluble and spongy in nature so get porous tablet</td>
</tr>
<tr>
<td>Sodium starch glycolate Explotab® Primogel®</td>
<td>Crosslinked starch</td>
<td>- Swells 7-12 folds in &lt; 30 seconds</td>
<td>Swells in three dimensions and high level serve as sustain release matrix</td>
</tr>
<tr>
<td>Alginic acid NF Satialgine®</td>
<td>Crosslinked alginic acid</td>
<td>- Rapid swelling in aqueous medium or wicking action</td>
<td>Promote disintegration in both dry or wet granulation</td>
</tr>
<tr>
<td>Soy polysaccharides Emcosoy®</td>
<td>Natural superdisintegrant</td>
<td></td>
<td>- Does not contain any starch or sugar. Used in nutritional products.</td>
</tr>
<tr>
<td>Calcium silicate</td>
<td>- Wicking action</td>
<td></td>
<td>Highly porous, optimum concentration is between 20-40%</td>
</tr>
</tbody>
</table>

### 1.4.8 Assortment of super disintegrant

The super disintegrant used in MDT formulation it influenced the rate of decomposition of tablets. However, the higher quantity of super disintegrants can disturb mouth sense, friability and tablet hardness. Therefore, varied ideal factors to be considered during selection of suitable super disintegrates for a precise preparation should:

- Generate prompt disintegration of MDTs
➤ Produces more strength to tablets, to overcome breaking of tablets during transportation

➤ Impart pleasurable mouth sensation to the patients

➤ Ameliorates the drift features of complete amalgamate

1.5 Mechanism of action

Following are the quartet major processes for tablets disintegration mentioned below:

1.5.1 Swelling

When MDT contact with water, the excipients start swelling due to this adherence of other ingredients is affected. The ingredients start breaking and followed disintegration of tablets. In this disintegration the porosity of tablet play vital role.

1.5.2 Porousness and capillary action (Wicking)

In this case the disintegrants breaks the MDT by porosity and capillary action. On placing the MDT into water, it gets absorbs in tablets and restores the aerate occupied on the fragments. This absorbs air weaken the intermolecular bond and start breaking of tablets into small fragments.
Fig 1.2: Mechanism of disintegration of MDTs
Fig 1.3: Mechanism of disintegration of MDTs containing fast dissolving granules
1.5.3 Disintegrating particle by repulsive forces

Guyot-Hermann recommended a particle repulsion theory on this non-
swellable disintegrant also leads disintegration of tablets. During study author
found that there is electric repulsive forces between particles were produced it
causes disintegration of tablets, and water is required for it.

![Disintegrating particle by repulsive forces]

Fig 1.4: Disintegrating particle by repulsive forces
1.6 Technology for mouth dissolving Tablets

When MDT placed into water, it enters rapidly into tablets across the matrix. This matrix produces spongy structure and results quick disintegration. By applying suitable disintegrating agent spongy structure of the matrix tablets can be improved. These exercising immensely polar-soluble excipients in the preparation.

Subsequent conventional techniques being used by different investigators to formulate mouth dissolving tablets:

- Lyophilization
- Moulding
- Sublimation
- Direct Compression
- Spray Drying
- Mass extrusion
- Nanonization
- Melt Granulation
- Cotton Candy Process
- Phase transition process
- Three – dimensional Printing (3DP)

1.6.1 Lyophilization or freeze-drying

The freeze-drying technique produces an shapeless spongy structure that can dissolve quickly. The carrier used play important role in liquefying of active drug after placing into water. Afterwards, blend is weighed for particular dose and placed the mixture into the wells for blister packs. To freeze dry the solution it passes through the liquid nitrogen freezing tunnel. After that chilled pustule flocks are kept in chilled cupboards to carry on the chill drying. The blister sealing is done by aluminum foil support. Lastly, the blisters of MDT are packed.22

Chief drawbacks of lyophilization technique are expensive cost of equipment and processing23.
1.6.2 Moulding

In this technique tablets disintegrate and dissolve quickly due to the occupancy of water-soluble components. The MDT are prepared by using compression pressure, the moistened powder mixture is melted into tablet. The compression applied in this technique is lesser than utilize in traditional pills densification. After that the solvent from mixture is evaporated by withering in air. The MDT prepared by this technique maintained its porous structure that increases the dissolution of doses. The chief drawbacks of this method are less mechanical strength and poor taste masking\textsuperscript{24-26}.

1.6.3 Sublimation

The extremely evaporative substances like benzoic acid, ammonium bicarbonate, camphor, ammonium carbonate, urea, naphthalene etc., are used in this method. These substances are added that evaporated rapidly in comparison to other excipients present in tablets. The blend obtained after this is compressed into tablets. Due to sublimation process the volatile substances present in the MDT are evaporated, and produces spongy matrix over tablets. The MDT formulated from this technique are extremely penetrable in nature and dissolve in saliva within 15 seconds\textsuperscript{24,25}. 
Fig 1.5: MDTs disintegrates by sublimation method
1.6.4 Direct compression

Today numbers of methods are available to manufacture tablets, but direct compression is simplest method. The tablets prepared from this technique are low cost compared to other technique. But in this technique the MDT are prepared by using super disintegrates and sugar based excipients.

1.6.5 Super disintegrate

The direct compression are used in the preparation of MDT by using super disintegrates. The super disintegrates mainly influences the rate of disintegration and dissolution\textsuperscript{25,26}.
1.6.6 Sugar based excipients

The expanding substitutes namely starch hydrolysate, dextrose, fructose, xylitol, isomelt, sorbitol, polydextrose, maltose and mannitol are used in the preparation of MDT. The aqueous solubility and sweetness property of bulking agent are most preferable. Moreover this type of bulking agent mask the bitter taste and produces pleasing mouth feel\textsuperscript{27,28}.

1.6.7 Spray drying

In this technique the MDT are prepared by compressing highly porous and fine powder into tablets. The most advantages of this method is that MDT disintegrates within 20 sec in an water\textsuperscript{29,30}.
Fig 1.7: MDTs prepared by spray drying
1.6.8 Mass extrusion

The mass extrusion is a process; the particular quantity of active blend is mixed with water soluble polyethylene glycol and methanol. After that, muffled aggregate removed by syringe to get a barrel shape of the products into even sections by applying the heated blade to form tablets. These dried barrel also used to smear the fragments for masking its acrid taste and produce pleasing relish of tablets\textsuperscript{31,32}.

1.6.9 Nanonization

The milling techniques are employed to reduced active ingredients in nano size. After stabilization of nano drug, these are then incorporated into MDTs\textsuperscript{12}.

1.6.10 Melt granulation

The hydrophilic waxy binders use in melt granulation process for the preparation of MDTs\textsuperscript{26}.

1.6.11 Cotton candy process

The cotton candy techniques is used to prepare MDTs containing saccharides or polysaccharides in amorphous form. The whole process is done by utilizing concurrent proceeding of flash liquefying and centrifugal force. The candy substances are with active ingredients and excipient. After that the blends are compressed into MDTs. The higher pressure are required during compression, this can increase the temperature of processing. The high temperature frontiers the benefit of this method for thermo stable substances\textsuperscript{33}.

1.6.12 Phase transition process

The phase transition process is used for the preparation of MDTs. In this method the low and high melting point sugar alcohols are mixed. No any special apparatus are requiring preparing the MDTs.
Fig 1.8: MDTs prepared by phase transition process

1.6.13 Three dimensional printing (3DP)

The 3DP method is used to manufacture MDTs by applying rapid prototyping (RP) technology. In this method the MDTs prepare can fast dissolve as compared to other technology.
### General Introduction

#### Table 1.2: Commercially available mouth dissolving tablet products

<table>
<thead>
<tr>
<th>Technologies</th>
<th>Trade name</th>
<th>Active ingredient</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Freeze drying</strong></td>
<td>Feldene Fast Melt</td>
<td>Piroxicam</td>
<td>Anti-rheumatic, non-steroidal</td>
</tr>
<tr>
<td></td>
<td>Claritin Redi Tab</td>
<td>Loratidine</td>
<td>Anti-histamine</td>
</tr>
<tr>
<td></td>
<td>Maxalt MLT</td>
<td>Rizatriptan</td>
<td>Anti-migraine</td>
</tr>
<tr>
<td></td>
<td>Zyperexia</td>
<td>Olanzapine</td>
<td>Anti-psychotic</td>
</tr>
<tr>
<td></td>
<td>PepcidRPD</td>
<td>Famotidine</td>
<td>Anti-histamine</td>
</tr>
<tr>
<td></td>
<td>Zofran mouth dissolve tablets</td>
<td>Ondansetron</td>
<td>5-HT₃ Antagonist</td>
</tr>
<tr>
<td></td>
<td>Zomig-ZMT</td>
<td>Zolmitriptan</td>
<td>Anti-migraine</td>
</tr>
<tr>
<td></td>
<td>ZelaparTM</td>
<td>Selegilline</td>
<td>Anti-psychotic</td>
</tr>
<tr>
<td><strong>Disintegrate Addition</strong></td>
<td>Tempra Quicklets</td>
<td>Acetaminophen</td>
<td>Anti-pyretic</td>
</tr>
<tr>
<td></td>
<td>Febrectol</td>
<td>Paracetamol</td>
<td>Anti-pyretic</td>
</tr>
<tr>
<td></td>
<td>Nimulide MDT</td>
<td>Nimesulide</td>
<td>NSAID</td>
</tr>
<tr>
<td></td>
<td>TorraxMT</td>
<td>Rofecoxib</td>
<td>COX-2 Inhibitor</td>
</tr>
</tbody>
</table>
### 1.7 Patented Technologies for preparation of MDTs\(^{37-44}\)

- Zydis Technology
- Orasolv Technology
- Durasolv technology
- Wowtab Technology
- Flash Dose Technology
- Oraquick Technology
- Ziplets/Advatab technology
- Lyoc Technology
- Pharmaburst technology
- Nanocrystal technology

### 1.8 Approaches for masking taste

In the current scenario, the pediatric and geriatric patients get inconvenience on taking tablets due to bitter and unpleasant taste of drug. Hence it is necessary required to mask the bitter taste of drug. This can increase enhance the patient acceptableness. It is considered that the oral dosage form should have less bitter for better acceptability. Presently various
methods has developed to reduce the bitterness of tablets and it enhanced the palatability of MDTs.

Generally, two methods are employed to overwhelm bitter taste of the active ingredients. In first method the drug dissolve in saliva, and after that equilibrium will occur between reduced solubility and bioavailability. The second method is applied to modify the drug interaction with taste receptors\(^{45}\).

The perfect taste masking protocol and preparation should produce following properties\(^{46}\):

- Machines and transforming phases should be lowest
- Least quantity of excipients required for an superlative formulation
- It does not produce any adverse and side effect
- Excipient should be easily available
- Reduces the manufacturing cost
- The processing can be done at room temperature
- It can be prepared easily and rapid

1.8.1 Methods to taste masking

The different approaches are present to disguise the unwanted flavor of the dosage forms. Some of these are covering of medicament fragments with inactive agents, Solid dispersion system, Microencapsulation, Multiple Emulsions, Inclusion Complex, Ion Exchange Resin, Mass Extrusion Method (Dispersion coating) and Prodrugs\(^{47}\).

1.9 Evaluation of mouth dissolving tablet

After complete formulation of mouth dissolving tablets it valuation is required for the quality assessment of tablets. Following methods can be applied to check the survival of tablets.

1.9.1 Angle of Repose

It can be measured by the funnel method. It is used to determine flow property of the excipients.
1.9.2 Bulk Density

It can be determined by using formula;

\[
\text{Bulk density} = \frac{M}{V}
\]

M – Mass of the blend

V – Tapped volume of the blend

1.9.3 Tapped Density

Tapped density is calculated by the formula:

\[
\text{Tapped Density} = \frac{M}{V_t}
\]

M – Mass of the blend

\(V_t\) – Bulk volume of the blend

Both the parameter is used to assess the porosity of the powder. This property can help in determining the settling of powder.

1.9.4 Carr’s Index

It represents the powder flow properties. It can be computed by the formula;

\[
\text{Carr’s Index} = \frac{(D_t-D_b)}{D_t} \times 100
\]

\(D_t\) – tapped density of the powder

\(D_b\) – bulk density of the powder

1.9.5 Hausner Ratio

It also reveals the flow properties of powder.

1.9.6 Weight variation of MDT

The weight variation is used to check the changing in weight of individual weight of tablets. It can be calculated by taking average weight of twenty tablets.
1.9.7 Dissolution test

The dissolution is used to determine the release of drug from tablets. The various solvent can use for dissolution of tablets. The solvents are as follows:

- 0.1N HCl
- Buffers
- Saline water
- Water

1.9.8 Thickness variation

The screw gauze micrometer is used to determine the thickness of the tablets. The thickness of tablets calculated by measuring the size of ten tablets and it means value indicate the thickness of individual tablets.

1.9.9 In-vitro dispersion time test

The in vitro dispersion time indicates the fully dispersion of tablets in 6 ml of water.

1.9.10 Packaging

The MDTs are commonly porous in nature and it required special packing to avoid damage of tablets during transportation or storage. For this special dome shaped blister packing are used for packaging of MDTs.

1.9.11 Size, shape, thickness and diameter

The physical evaluation of MDTs, the dimension and appearance can be supervised and regulated. The breadth of tablet can be measured by digital vernier calipers, by taking ten tablets. The thickness of tablets can be maintained uniform by the help of filling equipments.\textsuperscript{48,49}
1.9.12 Uniformity of weight

Minimum 10 tablets are weighed on electronic weighing balance, to measure the impact of MDTs. Thereafter the mean load of single tablet is calculated from the combined weight. This indicates the individual weight of tablet among whole batch.

1.9.13 Tablet hardness

The hardness of tablets is the strength requisite to split the tablets. The Monsanto Hardness tester, Pfizer hardness tester, etc are utilized to quantify the hardness of the tablet of each formulation. The values of hardness are expressed in Kg or pound\(^50\). The pressure needed to break the tablets is calculated as a function of hardness (kg/cm\(^2\)). The values obtained must meet the standard value.

1.9.14 Friability

The friability test apparatus (Campbell Electronics, India) are used to determine the friability of the tablet. Friability is to measure the extent of tablet breakage during physical stress conditions like packing, transportation etc. A sample of randomly selected 6 tablets was evaluated for friability using Roche friabilator at 25 rpm for 4 minutes. The percentage weight loss is calculated by measuring the total weight of 6 tablets before and after operation.

1.9.15 Wetting time

The ratio of wetting time and water absorption is significant parameters for mouth dissolving tablets evaluation. The filter paper is placed in Petridish containing water soluble dye solution (Sorenson’s buffer pH 6.8). After that, tablets are laid on the paper and the duration required for entire damping of the tablet is determined\(^51\).
1.9.16 Accelerated stability

The MDTs are used to special packing so that it can avoid moisture contamination. As per ICH guidelines, before post marketing of the MDTs it required to pass the stability test.

The tablets can kept in following temperature and duration to checks its stability:

- $40 \pm 1 \degree C$
- $50 \pm 1\degree C$
- $37 \pm \degree C$ and Relative Humidity= $75\% \pm 5\%$

1.9.17 Disintegration time

The disintegration duration for randomly selected six tablets is calculated by applying disintegration test unit (specified in I.P.-1996). The average time required for disintegration was calculated and compared with standards.$^{52}$

The acute sharp pain can be caused due to wounding burning, accident and bumping etc. The nervous system of human body play vital role in regulating the body pain. The severe or acute pain is generally controlled by analgesic drugs. But the elderly people and children occasionally get troubles in swallowing the tablets. While the bed-ridden patients get serious problem during swallowing tablets. Presently number of research has done in the novel drug delivery system (NDDS), to furnish reasonable remedy. The NDDS improved reputableness and potency of the medicament. It also ensures better patient compliance.

Here the mouth dissolving tablets bring boom in the market due to its easy and comfort administration of drug. The MDTs are the tablet which disintegrates in the patient's mouth in under a couple part of a minute. During disintegration of tablets it does not require water, or chewing. It provides the best treatment for the sufferer from dysphasia. The active ingredient present in mouth dissolving tablets is absorbed from the mouth, pharynx and
esophagus as the saliva passes into the stomach. This property can increase the bioavailability of drug compared to prevalent type of dosage. The precedence of MDTs is progressively being perceived in both commerce and academia.

1.10 **Analgesic and anti-inflammatory drugs**

The analgesic drugs are applied for the treatment of pain. The anti-inflammatory drugs are used for the reduction of inflammation in body. The numerous drugs belongs to NSAIDS category, and are effective in the treatment of pain and inflammation.

The conventional pain killer tablets are effective in reducing the pain, but these drugs are associated with lot of adverse effects. Following are the adverse effect and side effects produces to body on orally administering the drugs:

- Gastric ulcers
- Vomiting
- Constipation
- Nausea
- Diarrhea
- Headache
- Anemia
- Reduced hypertension action
- Decreases diuresis
- Rash
- Drowsiness
- Liver failure
Kidney failure

Increase bleeding time

Some of the above side effects and adverse effects can be minimized by using MDTs.

Hence an endeavor was performed to formulate mouth dissolving tablets with adequate mechanical property and to attain quicker disintegration in the oral cavity without water. Tolperisone a centrally acting muscle relaxant and Celecoxib a first cyclooxygenase-2 inhibitor, were selected for preparation of mouth dissolving tablets.
Table 1.3: List of generic and trade name of NSAIDS

<table>
<thead>
<tr>
<th>Generic Name</th>
<th>Tradename</th>
</tr>
</thead>
<tbody>
<tr>
<td>Celecoxib</td>
<td>Celebrex</td>
</tr>
<tr>
<td>Diclofenac</td>
<td>Cataflam, Voltaren, Arthrotec (combined with misoprostol)</td>
</tr>
<tr>
<td>Diflunisal</td>
<td>Dolobid</td>
</tr>
<tr>
<td>Etodolac</td>
<td>Lodine, Lodine XL</td>
</tr>
<tr>
<td>Fenoprofen</td>
<td>Nalfon, Nalfon 200</td>
</tr>
<tr>
<td>Flurbiprofen</td>
<td>Ansaid</td>
</tr>
<tr>
<td>Ibuprofen</td>
<td>Motrin, Tab-Profen, Vicoprofen (combined with hydrocodone),</td>
</tr>
<tr>
<td></td>
<td>Combunox (combined with oxycodone)</td>
</tr>
<tr>
<td>Indomethacin</td>
<td>Indocin, Indocin SR, Indo-Lemmon, Indomethagan</td>
</tr>
<tr>
<td>Ketoprofen</td>
<td>Oruvail</td>
</tr>
<tr>
<td>Ketorolac</td>
<td>Toradol</td>
</tr>
<tr>
<td>Mefenamic Acid</td>
<td>Ponstel</td>
</tr>
<tr>
<td>Meloxicam</td>
<td>Mobic</td>
</tr>
<tr>
<td>Nabumetone</td>
<td>Relafen</td>
</tr>
<tr>
<td>Naproxen</td>
<td>Naprosyn, Anaprox, Anaprox DS, EC-Naproxyn, Naprelan,</td>
</tr>
<tr>
<td></td>
<td>Naprapac (copackaged with lansoprazole)</td>
</tr>
<tr>
<td>Oxaprozin</td>
<td>Daypro</td>
</tr>
<tr>
<td>Piroxicam</td>
<td>Feldene</td>
</tr>
<tr>
<td>Sulindac</td>
<td>Clinoril</td>
</tr>
<tr>
<td>Tolmetin</td>
<td>Tolectin, Tolectin DS, Tolectin 600</td>
</tr>
</tbody>
</table>