FAST DISSOLVING TABLETS : A REVIEW

Mohd Arsh[1*], Jaya Martolia[2], Bhupendra Kumar[3]

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Abstract

Since the previous decade, oral administration has received substantially more attention for the treatment or management of disorders. Mouth dissolving tablets (MDTs), a novel idea in oral delivery, are now widely used. Mouth dissolving tablets are solid dosage forms that, when placed in the mouth for a brief amount of time without the use of water, dissolve and release the active ingredient. Geriatric, pediatric, and bedridden patients are particularly affected by it since they have swallowing issues, as do those with dysphasia. It is more practical for people on the go and busy patients without easy access to water. Superdisintegrants are used in a variety of technologies to make mouth-dissolving tablets.
Due to higher patient compliance, mouth-dispersing tablets are more dependable than traditional dosage forms like tablets and capsules. With the creation of an affordable and improved method of illness management and the avoidance of numerous issues associated to the other delivery systems, this sector has advanced.

[1*]Research Scholar, School of Pharmacy and Research, Devbhoomi Uttrakhand University, Dehradun, India.
[2]Professor, School of Pharmacy and Research, Devbhoomi Uttarakhand University, Dehradun, India.
[3]Assistant Professor, School of Pharmacy and Research, Devbhoomi Uttarakhand University, Dehradun, India.

Email: [1*]immd.arsh@gmail.com

Corresponding Author:
[1*]Mohd Arsh
[1*]Research Scholar, School of Pharmacy and Research, Devbhoomi Uttrakhand University, Dehradun, India.

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1. Introduction

The most common approach for administering medication for disease is through the oral channel. Tablets are a frequently prescribed dose form due to their self-administration accessibility, firmness, and ease of manufacturing. Patients, especially young children and the elderly, frequently have difficulty swallowing ordinary tablets, a problem that may get worse when traveling because of the lack of or limited access to water. The creation of mouth-dispersing tablets can address these issues with traditional dose forms.[1,2,3]

The most common approach for administering medication for disease is through the oral channel. Tablets are a frequently prescribed dose form due to their self-administration accessibility, firmness, and ease of manufacturing.[4,5] Patients, especially young children and the elderly, frequently have difficulty swallowing ordinary tablets, a problem that may get worse when traveling because of the lack of or limited access to water. The creation of mouth-dispersing tablets can address these issues with traditional dose forms.[6]

Patients with life-threatening disorders like neurological illness, radiation therapy, Parkinson's disease, and AIDS who experience the dysphasia condition can find great comfort from the mouth dissolving phenomena.[7] These patients experience difficulty while receiving novel dosage formulations like effervescent tablets or dry syrups because water consumption is required. However, mouth dissolving tablets improve patient compliance because they don't require patients to consume water when taking their medications.

Mouth dissolving tablets are also known as orally disintegrating tablets, quickly dissolving tablets, quickly melting tablets, etc.

The term "orodisperse" refers to a tablet that can dissolve fast in the mouth without the use of water, according to the European Pharmacopeia.[8]

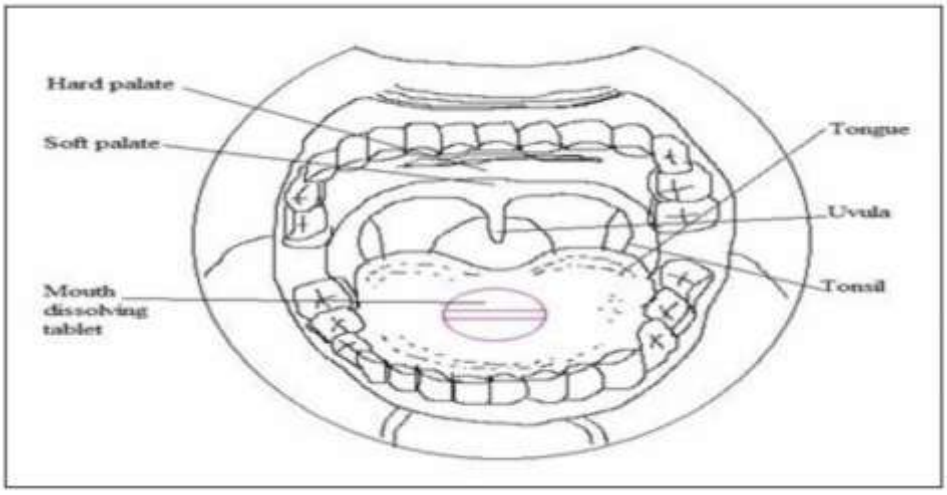

Figure 1: Administration of mouth dissolving tablets

Advantages of mouth dissolving tablets:

Mouth-dispersing pills are absorbed by the pre-gastric region, including the throat and esophagus, which causes a rapid onset of action [9,10]. This may increase an active pharmaceutical ingredient's bioavailability through dose minimization, clinical effectiveness, and minimal risk of side effects [11]. Especially in juvenile patients, the acceptability of medications with unpleasant tastes may be increased by mouth-dissolving tablets made with flavor masking ingredients. By using a standard dosage form, another convenience is

provided to prevent the obstruction of an oral route.[12,13]

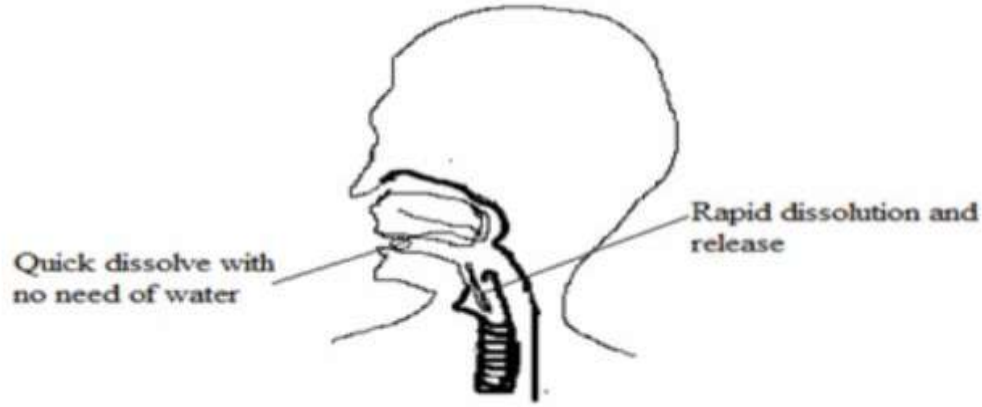

Figure 2: Dissolution and release mechanism of mouth dissolving tablets

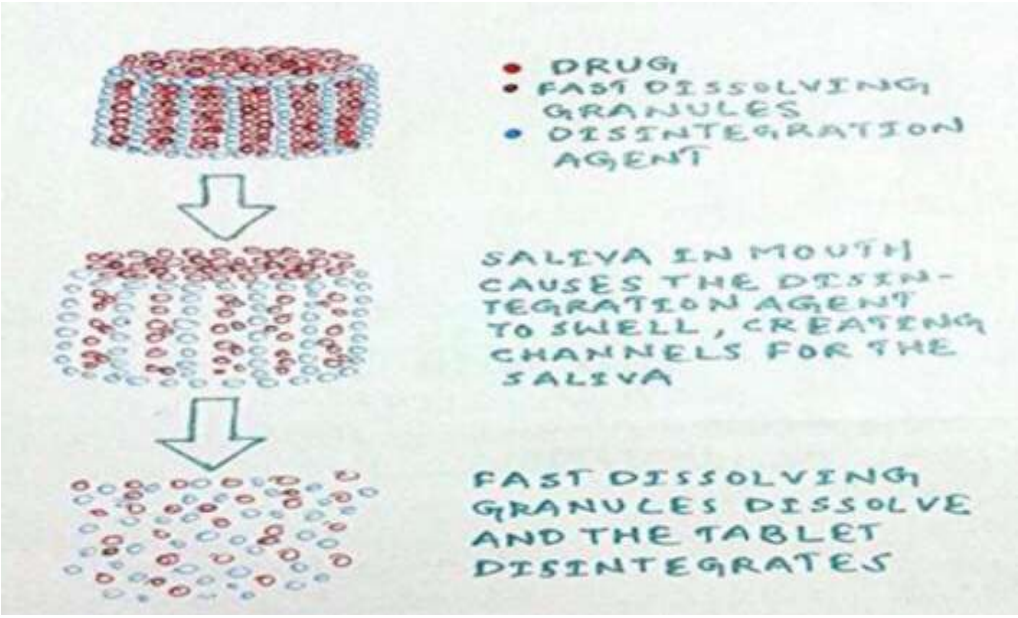

Figure 2: Disintegration of mouth dissolving tablets

Ideal Drug Characteristics for the Production of Orally Disintegrating Tablets:

Various criteria are taken into consideration while developing MDTs when choosing a medication candidate.

1. Substances that can permeate into the upper GIT epithelial layer (log P > 2).
2. Drugs with a brief half-life and frequent dosing.
3. Substances that, through first-pass metabolism, produce hazardous metabolites.
4. Drugs with a sustained or controlled release are inappropriate for MDTs.
5. The taste of very bitter medications makes them unsuitable for MDTs[14]

Potential Drug Candidates for Mouth Dissolving Tablets:

1. Non-steroidal acetaminophen, Piroxicam, Paracetamol, Rofecoxib, Nimesulide, and Ibuprofen are anti-inflammatory medications.
2. Lansoprazole and famotidine are anti-ulcer medications.
3. Mitraxepine and Fluoxetine are antidepressant medications.
4. Selegiline is an antiparkinsonian medication.

5. Sumatriptan, Rizatriptan benzoate, and Zolmitriptan are antimigraine medications.
6. Loratadine, Diphenhydramine, and Meclizine are anti-histaminic medications.
7. Ramosetoron HCl, Ondansetron, and Baclofen are antiemetic medication[15,16,17]

Mouth Dissolving Phenomenon

When designing pills for oral administration, superdisintegrants are taken into much greater account. By inducing swelling and water absorption in the pill, they offer quick disintegration. The superdisintegrants' swelling process moistens the carrier's surface, which speeds up tablet dissolving and results in higher dissolution rates. The swelling capacity in the dissolution media and the density of the generated matrix both affect how well superdisintegrants operate. A higher level of matrix disintegration is caused by higher swelling capacity and density.[18,19]

Superdisintegrant Mechanisms

They run on four fundamental mechanisms:

1. Swelling: Through this process, certain disintegration ingredients, such as starch, when in contact with water, impart the dissolving action and cause the pill to break down. Sodium starch glycolate, for instance, or Plantago Ovata. [20]

2. Porosity and Capillary Action (Wicking): Some superdisintegrants disintegrate due to porosity and capillary action. The disintegrating particles work to increase porosity, which creates pathways for liquid to permeate into tablets. The liquid is then exhausted by capillary or wicking activity, which causes the breakdown of inter-particle bonding and finally the disintegration of the tablet. For example: Crosspovidone and Crosscarmellose.[21]

3. Deformation: The starch grains distorted when pressure was applied to them, and they returned to their normal shape when the pressure was released. However, they permanently distorted when they were compacted into tablets, releasing their energy when in contact with water. [22]

4. Because of Particle/Particle Disintegration Repulsive Forces: This process is connected to disintegrants that cannot swell. Guyot-Hermann responded with the particle repulsion theory. Disintegration electric repulsive interactions between the particles, so the theory goes, are what cause the water. Many different processes are thought to be used by the majority of disintegrants. However, it is the outcome of the interactions between these important systems.[23]

Table 1: List of commercially available superdisintegrants

S. No.	Superdisintegrants	Mechanism of action	Properties	Available grades
1	Cross-linked Alginic acid	Upon hydration, wicking activity causes a quick bulge.	Cohesion that is loose in a wet and dry medium	Alginic acid, Satialgine
2	Cross-linked PVP	acting by capillary action	Water-insoluble and naturally spongy	Kollidon, POlyplasdone, Crosspovidone, Crosspovidone M
3	Cross-linked starch	expands seven	gives a matrix-	Primogel,

		to eleven folds in less than 30 seconds.	based continuous release that swells in three dimensions.	Sodium starch glycolate, Explotab
4	crosslinked polymer of Polycarboxylic acids	Very high tendency to expand when hydrated, whether in touch with water or internal fluids	improves the effective surface area for the active compounds' absorption	Kyron T-314
5	Cross-linked cellulose	in less than 10 seconds, swells 4 to 8 times. expanding and wicking	Swelling is a two-dimensional phenomenon that is used in direct compression or granulation.	Croscarmellose, Ac-Di-sol, Nymce ZSX, primellose, Solutab, Vivasol

Making of tablets for oral dissolution:

Different specialised methods, including lyophilization, spray drying, direct compression, sublimation, mass extrusion, cotton candy, etc., were used to manufacture MDTs.

Nowadays, lyophilization or freeze-drying is routinely considered. With the use of sublimation after product freezing, the product is transformed into a porous structure that is simple to dissolve. The medicine is mixed with a carrier, then poured into a blister that has already been produced. These blisters are held in a tray that is taken through a liquid nitrogen tunnel to completely freeze the dispersion before going through a freeze dryer.

Blister sealing processes use aluminium foil as the backing material.[24]

Zydis technology (ZT), based on the freeze-drying process's fundamental premise, is a patented method for producing mouth-dissolving tablets. Ondansetron, loperamide, piroxicam, rizatriptan, lorazepam, domperidone, oxazepam, olanzapine, and famotidine are just a few of the active pharmaceutical ingredients found in thirteen items that were produced utilising this method [27].

Using this strategy, numerous excipients with distinct functions are combined to meet the various formulation aims. Gelatin, for instance, gives tablets their strength and rigidity. Mannitol or sorbitol increase the crystallinity and hardness of the matrix, which is crucial for increased palatability. Glycine plays a part in preventing packaging from shrinking during production or storage.

Using xanthan gum or acacia, the medication particles are uniformly dispersed. In addition to these, preservatives such parabens, permeation enhancers for trans-mucosal permeability like sodium lauryl sulphate, pH adjusters like citric acid, and the most crucial excipient flavours and sweeteners are utilised, all of which promote patient compliance.

The primary advantage of this approach is its swift melting effect, as evidenced by its speedy disintegration and satisfying mouthfeel. However, it is relatively expensive, takes a lot of time, and because the product is unstable and fragile, traditional packaging is not appropriate.[28] .

By using the lyophilization process, Shoukri et al., [2009] created the orally

disintegrating tablets of nimesulide (NM). The medicine with the worst solubility and bioavailability is NM. The NM oral disintegrating tablets (ODTs) dissolve in a matter of seconds and disintegrate much more quickly than the generic powdered medicine and standard commercial tablet. The created formulation demonstrated increased in vivo bioavailability of up to 60% and in-vitro disintegration time less than 10 seconds.

%. Various disintegration accelerators were used in this, including PEG 400, PEG 4000, PVP K25, PVP K30, PVP K90, Tween 20, Tween 80, etc., with PVP K90 demonstrating an especially high rate of disintegration extremely low wetting time of 5.53 sec.[29]

Despite significant technological advancements in the production of MDTs, direct compression is still extensively employed since it is both relatively affordable and straightforward. For the direct compression production process, tablet excipients with favourable micrometric characteristics, such as compression, increased flow, and disintegrating effect, are utilised. The usage of disintegrants affects the pace of disintegration, which increases dissolution when water-soluble excipients are present. Superdisintegrants' integration is more important in this phase.[30]

The main determinants of tablet disintegration time are superdisintegrants. Tablet disintegration time increases with decreased superdisintegrant concentration and vice versa as long as the concentration is below a critical level; it stays constant at higher concentrations.[31] There are two different kinds of disintegrants used: the first is a disintegrating agent like modified cellulose that has a high swelling force, and the second is a swelling agent like starch that has a low swelling force.[32] In addition to these, effervescent agents are employed in the genesis of CO_2, which serves as the mechanism for quick disintegration.[33,34]

The active medicinal components are combined with polymers like methylcellulose, acrylates, etc. in conjunction with tablet excipients like mannitol, magnesium oxide, etc., and then continuously stirred. These excipients work as release coordinators for the active medicinal compounds that are encapsulated in polymers. It was then dried for about an hour at 50 °C, de-lumped, and taken up again to dry for a second time at the same temperature before being passed through an 8 mesh screen size and dried for an additional hour at 60 °C.

Tablets are created by combining these shaped microparticles, effervescent agents, and other excipients. The use of sugar-based excipients such sorbitol, fructose lactitol, maltose, etc. can also be used to mask tastes. These substances have a very hydrophilic nature and provide sweetness, creating a nice mouthfeel.

Mizumoto [1996] described two types of saccharides, one of which is very soluble, such as lactose and mannitol, and the other of which has a short dissolving time, such as maltose.[35]

In order to increase therapeutic efficacy via direct compression technique, Singh et al. [2012] designed a Zolmitriptan mouth dissolving tablet containing superdisintegrants such as Kyron T-314, Crosspovidone, Croscarmellose sodium, and sodium starch glycolate. The formulation made using kyron T-314 showed a quick 35-second disintegration time. These mouth-dissolved Zolmitriptan tablets on the market today offer a quick beginning of action, a higher bioavailability, and good stability.[36]

Flurbiprofen solid dispersion with PEG 6000 was created by Jain et al. in 2016, and utilising superdisintegrants including sodium starch glycolate, cross carmellose sodium, and Kyron T-314, this was further compressed into mouth-dissolving tablets. The prepared lots of MDTs were evaluated

for their micrometric properties, drug content, in-vitro drug release profile, thickness, hardness, weight fluctuation, wetting time, and disintegration time.

With a wetting time and disintegration time of 28.3 and 38.3 seconds, respectively, the KT9 formulation containing 4% Kyron T-314 demonstrated the best performance among them. Over the course of 30 min 37, the KT9 formulation demonstrated a greater drug release of 99.96% compared to 54.24% for the conventional formulation.[37] An active delivery system for the control of hypertension was developed by Joshi et al. in 2018. The goal of developing the orodispersible tablets (ODTs) containing telmisartan was to achieve improved solubility leading to a higher bioavailability profile. For the formulation of the ODT system, various ratios of Telmisartan and PEG 6000, including 1:1, 1:2, 1:3, 1:4 and 1:5, were chosen.

Each medication and polymer mixture was made in batches, and the final solid dispersion was then crushed into tablets using a direct compression technique. Preformulation analysis was done on the materials' solubility profile, drug content, Fourier Transform Infrared (FTIR) spectroscopy, and Differential Scanning Calorimetry (DSC). A following compression stage was chosen with a drug-polymer ratio of 1:4.

Micrometric analysis, thickness, hardness, weight variation, wetting time, disintegration time, drug content, and in-vitro drug release profile were all performed on the manufactured batches of ODTs. The evaluation statistics for all batches were good. However, formulation TF3 with 6% kyron T314 produced the best results, with wetting and disintegration times of 29.3 seconds and 24.1 seconds, respectively. Over the course of 30 minutes, this formulation demonstrated a superior drug release of 99.93%.[38]

Another method of producing MDT uses the spray drying process to create highly porous, fine powder in reaction to the solvent evaporating quickly. Using this method, tablets that dissolve quickly are produced. The major constituent is retained in an aqueous solution with the support matrix and other components, which forms a porous and fine powder, and the tablets are immediately pierced.[39] In this procedure, both hydrolyzed and non-hydrolyzed gelatin is discarded as a matrix. Mannitol serves as a bulking agent and sodium starch glycolate and croscarmellose serve as disintegrants. The addition of acidic or alkaline substances, such as sodium bicarbonate or citric acid, enhances the dissolution and disintegration phenomenon. Additionally, the excipient combination was spray-dried to create a porous powder substance that was later utilised for tablet compression [40].

The sublimation method is an alternative technique to spray drying for the high porosity mouth-dissolving tablets. The sublimation method involves compressing all the volatile components, together with other excipients, into tablets to create a porous matrix. In this method, inert substances like camphor, urea, ammonium bicarbonate, and naphthalene are employed. Solvents like benzene, cyclohexane, and others also contribute to the matrix's porosity.[41] Using two techniques, including the sublimation technique and freeze-drying using Ac-Di-Sol as a superdisintegrant and camphor, menthol, and thymol as a subliming agent, Elbary et al. [2012] developed orodispersible tablets containing meloxicam.

Since meloxicam has a low solubility in water (12 g/ml), it dissolves poorly when wet and has variable bioavailability as a result. The formulation with the highest camphor content has the shortest wetting and disintegration times (9 and 10.1 seconds, respectively). The prepared orally disintegrating pills dissolve within a few

seconds without the need for water, improving absorption and meloxicam bioavailability.[42]

Incorporation is one method used in the manufacture of mouth-dissolving tablets using a polyethylene glycol and methanol combination. A syringe or other tool is used to inject this solvent system, giving it a cylindrical shape. Tablets will be created by sectioning this using a sharp blade. This is also used 43 to disguise the taste of harsh medications.[43]

The main procedure for weakly water-soluble medicines is nanonization. Wet media milling techniques are used in this method to decrease the drug's particle size. The technique involves shearing the drug particles from micron to nano size using a water-based media milling process. Stabilisers are employed to stop surface adsorption from clumping the nanocrystals together. 90% of nanoparticles in a stable nanoparticle dispersion have a diameter of less than 400 nm, with the mean diameter often being less than 200 nm.[44]

Using nano-crystal technology, Lai et al. [2011] created orally disintegrating tablets (ODTs) to improve the lipophilic, poorly soluble medication piroxicam's (PRX) dissolving characteristics.

The formulation showing a high percentage of poloxamer 188 release from the ODT in less than 60 minutes.[45]

Table 2: Patented technologies for mouth dissolving tablets

S. no.	Technology	Method	Active Moeity	Company
1	WOWTAB®	Direct compression	Famotidine	Yamanouchi Pharma Technologies, 1050 Arastradero Road, Palo Alto, CA, USA
2	ORASOLV®	Direct compression	Paracetamol	Cima Labs, Inc., 10000 Valley Hill Road, Eden Prairies, MN, USA
3	DURASOLV®	Direct compression	Zolmitriptan	Cima Labs, Inc., 10000 Valley Hill Road, Eden Prairies, MN, USA
4	FLASHTAB®	Direct compression	Ibuprofen	Prographarm, ChaueauneufEn-Thymeraia, Fran
5	LYOC®	Lyophilization	Phlorglucinol hydrate	Farmalyoc, 5AV Charles Marting, MaisonsAlfort, France
6	QUICKSOLV®	Lyophilization	Risperidone	Janssen Pharmaceutica, 1125 TrentonHarbourton Road, Titusville, NJ, USA
7	ZYDIS®	Lyophilization	Loratidine	R. P. Scherer, Frankland Road, Swindon, UK

8	FLASHDOSE®	Cotton Candy Process	Tramodol hydrochloride	Fuisz Technologies, 14555 Avion At Lakeside, Chantilly, VA, USA

The methodology used to make cotton candy is distinct from all the others. The technology used to create FLASHDOSE® mouth-dissolving tablets is Shear-formTM and Ceform TITM. The disagreeable taste of the active medicinal ingredients is eliminated as a result. Shearform technology was used to create "Floss," a combination of manufacturing excipients used either alone or with active medicinal components. The manufacture of floss, which resembles cotton candy fibres, uses saccharides such sucrose, dextrose, lactose, and fructose. For that, have been applied at a temperature of 180-266 °F.[48] The benefit is that because the tablet is porous and comes into touch with saliva, the sugars dissolve, giving off a very pleasant sensation.

Evaluation of MDTs

Tablets that dissolve in the mouth are assessed based on a number of factors, including their hardness, friability, weight variation, medication content, etc. In addition to these traditional evaluation criteria, there are several particular criteria that are crucial in determining if MDTs are effective for medication administration. Wetting time, dissolution time, dissolution study, and moisture uptake study are some of these metrics.

Because MDT dissolves quickly in the mouth after being placed there, the wetting time of the mouth dissolving tablets is very long.

Lower wetting time results in very quick MDT breakdown, hence it's crucial in the production of mouth-dissolving tablets. 10 ml of distilled water containing eosin, a water-soluble dye, was put in a 10 cm diameter Petri dish to measure the wetting time. The time necessary for water to touch the higher surface of the tablet was noted after the tablets had been carefully positioned in the centre of the Petri dish. This is referred to as wetting time.[51]

For MDTs, the disintegration test is also frequently used. The USP disintegration test instrument is used to calculate disintegration time. Each batch of six tablets includes a disintegration test. The disintegration test is conducted in 900 ml of pH 6.8 simulated saliva fluid at a temperature of 37 0.5 °C and at a rate of 30 2 cycles/min.[52]

For tablets that dissolve in the mouth, a dissolution study is crucial. Using the tablet dissolve test apparatus (USP XXII type) at 50 rpm, an in-vitro dissolution study of mouth-dissolving tablets is performed. The dissolution medium is phosphate buffer pH 6.8, and the temperature is held constant at 37 0.5 °C. Samples are taken out at various times and subjected to an appropriate analytical technique.[53]

Several excipients are hygroscopic in nature, thus in addition to these mouth-dissolving tablets, tests on moisture uptake are also conducted using them. Ten tablets of calcium chloride are chosen at random from the desiccator and kept there for 24 hours at 37 °C.

The tablets are then weighed and exposed to a relative humidity of 75% at room temperature for two weeks.

For three days, sodium chloride is placed at the bottom of the desiccators to maintain a relative humidity level of 75%. One superdisintegrant deficient tablet is preserved as a control group to assess how other excipients absorb moisture in the tablet.[54]

2. conclusion

On contrast to more traditional dosage forms like tablets and capsules, mouth-dissolving tablets are highly preferred on the market today. In a drug delivery system, patient compliance and satisfaction are crucial. In addition to being advantageous to dysphasic individuals, mouth-dispersing tablets are cost-effective because they dissolve in the mouth within a few minutes and release active ingredients. The latest manufacturing techniques result in tablets that act quickly, have a higher bioavailability, have less side effects, and are safer.

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