



A REVIEW ON DIFFERENT PHARMACEUTICAL TECHNOLOGY AND DOSAGE FORM USED IN TREATMENT OF DEPRESSION

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ABSTRACT

Because of its durability and patient acceptability, the tablet is the most commonly used dosage form out of all those that are available. A coating plays a crucial role in the tablet's formulation because it influences aesthetic qualities like colour, texture, mouth feel, and taste masking. The goal of the current work is to provide an in-depth analysis of the formulation, characterization, and difficulties encountered when creating tablets in tablet dosage form. Tablets are the most frequently prescribed dosage form because they provide a convenient method of drug administration, ensure dosage uniformity from tablet to tablet, are stable over long periods of time and under various storage conditions, and can be made using high-speed compression, labelling, and packaging equipment. The goal is to improve acceptance and bioavailability through technological advancements and modifications to the basic compressed tablet. Many newer, more effective tablets have been developed to design a delivery system that is reasonably straightforward to administer. Osmotic pump systems operate in the same manner as other membrane-controlled release medication delivery systems. The medicine is contained in a water-soluble tablet core, which will solubilize or suspend the drug when exposed to water. Also advantageous is a multi-layer tablet dosage form, as opposed to the more common mono-layer tablet. Due to constant therapeutic levels of the drug, the gastro retentive dosage form in FDDS increases bioavailability, therapeutic efficacy, and permits a dose decrease. So, in this review article, we will examine the principles of tablets, their technology, and the different kinds of systems that are used with commercially accessible goods in a range of dosage forms.

Key-words- Dosage Form, Tablet, Excipients, Methodology manufacturing, Nanotechnology

DOI Number:10.14704/nq.2022.20.8.NQ44472

NeuroQuantology 2022; 20(8): 4402-4422

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1.1 DEPRESSION

One of the common illnesses that result from the way we live now and is now one of the reasons people visit a psychiatrist is depression. Depression is a result of psychological issues. [1].

Different types of depression may exist. Lack of appetite, sleep, work, eating, and withdrawal from social activities are signs of depression. Dysthymia is another form of depression that has persistent, long-lasting symptoms that keep the patient actively



engaged but who nevertheless experiences occasional depressive episodes. Manic and bipolar depressions are two types of depression that occur when a person has abrupt changes in mood (from normal to extreme). The ability to judge, think, and behave socially may be impacted by this type of depression, which is frequently accompanied by mania. [2].

Symptoms of depression:

Symptoms of depression may be as:

- i. Change in mood,
- ii. Negative thinking
- iii. Feeling himself/herself guilty and helpless
- iv. Withdrawal of social activities, lack in other activities that he or she enjoyed, including sex,
- v. Lack of sleep.
- vi. Lack of appetite or loss in a loss.
- vii. Suicidal tendency.
- ix. Feel a lack of energy.
- x. Lack of concentrating on work, lack of remembering or making decisions [3]

1.2 INTRODUCTION OF MOUTH DISSOLVING TABLET

One of the most popular drug delivery routes in the area of pharmacy is the oral route. The oral route is well-liked since it is straightforward, adaptable, practical, and has great patient compliance. However, it has been noted that oral dosage forms, including tablets and capsules, have various restrictions on the medications, including:

- Undergoes first pass effect.
- Cause gastric degradation.
- Have a short half-life.
- Patients don't want to swallow tablets.

These drawbacks can be overcome by creating novel drug delivery systems, such as mouth-dispersing tablets, mouth-melting tablets, mouth-dispersing films, etc., which increase patient compliance while also increasing safety and efficacy of the pharmacological moiety. Mouth dissolving

tablets (MDTs) are solid unit dosage forms that are designed to quickly dissolve in the mouth without the help of water within a few seconds to provide a speedier onset of action. The US Food and Drug Administration (US FDA) states that "MDT is a medicine including solid unit dosage form which demonstrates fast breakdown, usually within few seconds, when it is placed upon the tongue." One of the most popular drug delivery routes in the area of pharmacy is the oral route. through the mouth Within a few seconds, without the help of water, to provide a quicker start of effect. The US FDA states that MDT is a medication containing solid unit dose form that rapidly disintegrates when placed on the tongue, often within a few seconds [4]. Patients who have trouble swallowing traditional immediate release tablets, such as children and the elderly, benefit greatly from mouth-dispersing tablets. The reason MDTs function so quickly is because of their speedy disintegration, which leads to quick dissolution and quick absorption. MDTs also offer precise dosing, high stability, and convenience of production, packaging, and patient handling. Therefore, delivering MDT to patients who are young, old, or have mental health issues is advantageous [5].

1.2.1 Mechanism of a Mouth dissolving tablet

1. Due to the inclusion of super disintegrants, which swell and form pores for salivary fluid to quickly penetrate within the tablet and cause swelling and pressure, MDTs disintegrate quickly when in contact with salivary fluid in the oral cavity.

2. Mechanisms that are responsible for the rapid disintegration of tablets are as:

- The high swelling ability of disintegrants used
- Chemical reaction
- Capillary action [6,7]



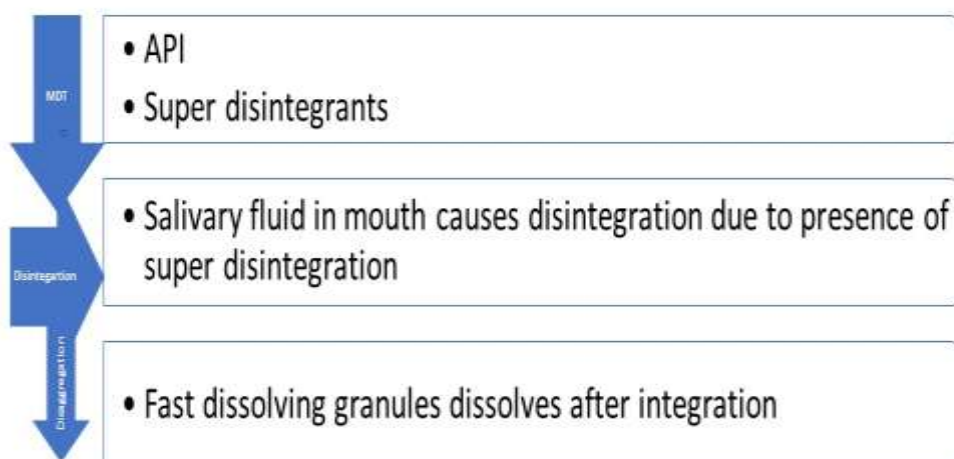


Fig. 1 Mechanism of tablet disintegration

1.2.2 Need of developing MDTs

In order to improve patient compliance because they have a swallowing issue, like geriatric patients, MDTs are designed to be non-invasive delivery devices. An eight-year-old pediatric patient prefers a more convenient MDT dosage form than a liquid dosage form, and a middle-aged breast cancer patient who is receiving radiation therapy may feel too sick to swallow an H2 histamine receptor antagonist -blocker. MDTs are also helpful for patients who have difficulty swallowing or chewing solid dosage forms.

Industrial and market need for MDTs

Regarding pharmacological safety and efficacy, MDTs are comparable to traditional immediate-release tablets. Today, innovative patented methods like Flash tab technology, Zydis, Wow Tab, etc. are being researched to create MDTs. Due to enhanced patient compliance, these dosage forms are gaining market share daily and are quickly becoming the preferred dose form. [9, 10]

1.2.4 Ideal properties of Mouth Dissolving Tablets

1. It doesn't require water because it dissolves, disperses, or disintegrates in the mouth after a brief period of time.
2. It has a satisfying mouth feel.

3. Because it possesses taste-masking properties, it can be utilized to give bitter medications.
4. It needs to be mechanically strong enough to absorb shocks while being handled and transported. It must be able to handle heavy drug loading.
5. It must be clean and leave no trace.
6. It must be able to withstand environmental humidity and temperature. [11, 12]

1.2.6 Challenges in preparation of MDTs Palatability

Because the majority of medications have an unpleasant or bitter taste, creating a palatable MDT is the biggest issue. To increase patient adherence, the bitter or unpleasant taste of an MDT must be covered up since as soon as it is delivered, it quickly disintegrates in the mouth and comes into touch with taste buds.

Mechanical strength

It is crucial to manufacture MDT at low compression force since high compression forces can influence the friability and hardness of the MDTs and prevent them from disintegrating in the oral cavity. With the help of cutting-edge processes like Wow tab and Duracell technologies, MDTs can be used to create tablets that are sufficiently strong mechanically and less friable.



Hygroscopicity

As it may damage the integrity of the tablet under typical temperature and humidity settings, this is one of the key factors that must be taken into consideration. Thus, controlled relative humidity should be the environment in which MDTs grow.

Amount of drug

Each unit dose form, such as MDTs, has a different amount of the medicine. For lyophilized formulations, the recommended medication dose is typically between 60 and 400 mg for soluble pharmaceuticals and 400 mg for insoluble drugs. When creating films or wafers that dissolve quickly, this feature is essential.

Aqueous solubility

To ensure quick dissolving in the mouth while creating an MDT, it is crucial to choose a water-soluble medication. By using strategies to increase solubility, such as solid dispersion, hot melt extrusion, the addition of hydrophilic excipients, the use of sophisticated methods, etc., medications' solubility can be increased.

Size of tablet

When handling and administering a tablet to a patient, its size is crucial. It becomes challenging to formulate and handle a tablet with inferior tablet size. The tablet's size is typically calibrated between 7-8mm. [13]

Faster disintegration

A tablet's rapid disintegration time determines how quickly it starts working. Because the drug dissolves in the oral cavity more quickly with faster disintegration, the effects start to take effect more quickly.

Packaging design

One of the crucial factors to be considered while studying a pharmaceutical's performance is its packaging, which is crucial for both its handling and the protection of the dosage form from moisture and the outside environment. [14]

1.2.7 Advantages of MDTs

1. The use of MDTs increases patient compliance.
2. Through widespread oral cavity absorption, MDTs enhances bioavailability, lowers the dose, and enhances clinical performance.
3. MDTs have the benefit of being simple to administer to elderly and paediatric patients who have swallowing difficulties.
4. It also aids in boosting psychiatric patients' compliance.
5. A patient can be administered while on the go without the requirement for water.
6. Compared to other liquid dosing forms, MDTs aid in administering more precise doses. [15]

Advantages of MDTs over other dosage forms

- MDTs demonstrate good stability, dosage accuracy, manufacturing ease, and handling ease.
- It can be administered while travelling without the need for water.
- It is a desirable dose form for patients with pediatric and geriatric conditions.
- Due to its quick disintegration and dissolution, it has a rapid beginning of effect.
- It is appropriate for bitter medications since tastes and sweeteners can be added to it to cover the taste.
- As medications are absorbed from the mouth, pharynx, and esophagus, it increases their bioavailability.
- As a result of pre-gastric absorption, it exhibits less hepatic metabolism. [16]

1.2.8 Limitations

MDTs typically have low mechanical strength and hardness. As a result, it needs to be handled carefully. It occasionally leaves behind a bad taste or grit. It is not adequately constructed. MDTs are appropriate for medications with higher doses, such as antibiotics. It is not appropriate for a condition like Sjogren's syndrome, which causes people to have less saliva in their mouths. [17]



1.2.9 Disadvantage

1. due to their hygroscopic nature MDTs are stored carefully in a dry place.

2. MDTs are also required specialized packaging due to their less mechanical strength, and stability problems. [18]

1.2.10 Technologies adopted for MDTs

Granule aggregation

There are several mechanisms of agglomeration binding:

1. Solid bridge formation

Sintering may result in the solid bridge forming. Chemical processes and the application of a hardening binder both have the potential to produce solid bridges. The process of sintering required heating a material mixture to about two-thirds of its melting point, followed by softening, which results in atoms diffusing from one particle to another.

7. Force of adhesion and cohesion

The force that draws other molecules of the same type together is known as the force of cohesion. While the force causing the attraction of various sorts is known as the force of adhesion Substances.

3. Surface tension and capillary force

Liquid bridges may form in the powder blend if there is free water present or capillary condensation. Solid bridges are formed as a result of these forces.

4. Force of Attraction

It has been proven that incredibly small particles can be held together by a few weak forces that emerge between them. Vander Waals forces, for instance, draw the particles very closely together.

5. Interlocking Bonds

When the particle solids are stretched, this bonding takes place. Agglomeration at very high pressure may cause interlocking bonds to form. This bonding may take place in materials that are both hard and plastic.

6. Wicking

Due to the presence of some specialist excipients, such as starch, which is employed as a disintegrant, this occurrence results in the creation of capillaries inside the dosage form, which facilitates the disintegration of tablets.

7. Swelling

One of the main factors contributing to the disintegration of tablets is swelling. These disintegrants swell, causing the tablet to disintegrate as a result of internal pressure. [19]

1.3 Super disintegrants

The disintegration and breakdown of MDTs are caused by disintegrants. Therefore, it becomes crucial to choose an appropriate disintegrant that guarantees quick disintegration at an optimal concentration to aid in the drug's breakdown. The combination impact of swelling and water absorption makes super disintegrants the finest polymer for assisting in the fast disintegration of MDTs. Compared to normal disintegrants, which are employed in immediate-release pills, supradisinterants have a multiplied potential to swell. If super disintegrants are present in sufficient concentration, the tablet disintegration time may be adversely impacted. Crosslinked polymers are examples of several typical universal super disintegrants. Croscarmellose sodium, crospovidone, carmellose calcium, sodium starch glycolate (SSG), and other super disintegrants are examples. [20]

These super disintegrants have increased mechanical strength and disintegration efficiency, making them more efficient at lower concentrations. Superdisintegrants must be applied in MDTs with modest concentrations, typically 1 to 10% w/w. Since super disintegrates' particles are tiny and porous, they may encourage quick decomposition of MDTs in the mouth without leaving a bad aftertaste. [21]

1.3.1 Ideal properties of Super-disintegrants

1. It must have a high hydration capacity.
2. It must have good flow properties.



3. It should not form complexes with the drugs.
4. It should not leave any unpleasant taste in the mouth.
5. It should be inert.
6. It should be nontoxic.
7. It should be economic.

Factors affecting the selection of Super disintegrants

- Amount of disintegrants present in the formulation.
- Tablet hardness.
- Method of addition and mixing.
- Drug nature.
- Flow property.
- Compression property
- Mouth feel.

1.3.2 Method of Incorporation of super disintegrants

Super-disintegrants can be incorporated in a dosage form in three ways as mentioned below:

Intragranular – Super-disintegrants are added to other excipients or granules in this manner, which is known as intragranular. Because of this, super disintegrants are included in the produced granules.

Extra granular- Super-disintegrants are mixed into the prepared granules or powder blend in the extra-granular procedure, which is done right before compression.

Intra and extra granular both- This method of super-disintegrant addition is the most popular. Super-disintegrants, both intra- and extra-granular, are introduced to the powder mixture in this approach right before compression and during granule formation.

1.3.3 Different Types of Superdisintegrants

There are two types of Super disintegrants:

1. Natural Super-disintegrants
2. Synthetic Super-disintegrants

Natural Super-disintegrants

These super disintegrants are of natural origin. These super-disintegrants are economic, readily available, non-toxic, inert, and non-irritating. For example gums and mucilages like fenugreek seed, gum karaya, gum of locust bean, alginates, xanthan gum, chitin and chitosan, gellan gum, pectin, etc.

Synthetic Super-disintegrants

These are the cross-linked polymer of naturally occurring disintegrants. For example, croscarmellose sodium (Ac-Di-Sol) is derived from cellulose, sodium starch glycolate (Primojel and Explotab) is derived from starch, and crospovidone (Polyplasdone XL) is derived from povidone.

1.3.4 Advantages of Synthetic Superdisintegrants

1. These are used in a low amount as compared to disintegrants.
2. It does not affect tablet compression ability and flow property of granules.
3. These are effective when added intragranular. [22, 23]

1.3.5 Mechanism of disintegration by super-disintegrants

Super disintegrants work by five mechanisms as mentioned below:

1. Swelling
2. Porosity and Capillary Action (Wicking)
3. Deformation
4. Due to disintegrating particle/particle repulsive forces
5. Enzymatic reaction

1. Swelling: One of the factors that causes the pills to dissolve is swelling. A tablet breaks when it comes into touch with water because the disintegrants swell. Sodium starch glycolate, for instance.



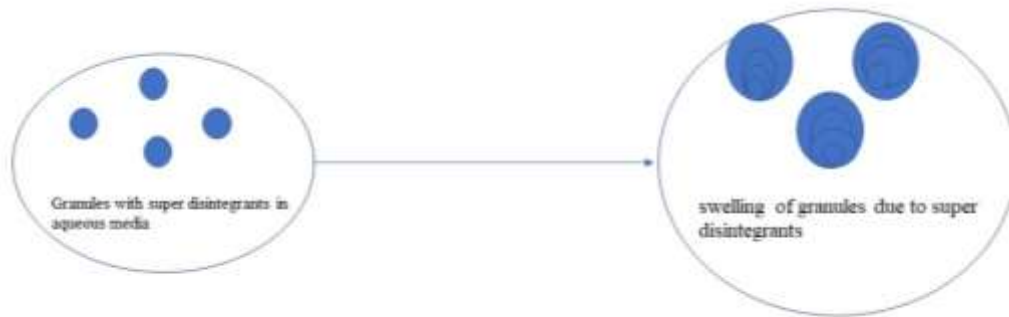


Fig. 3 Swelling of granules due to super disintegrants

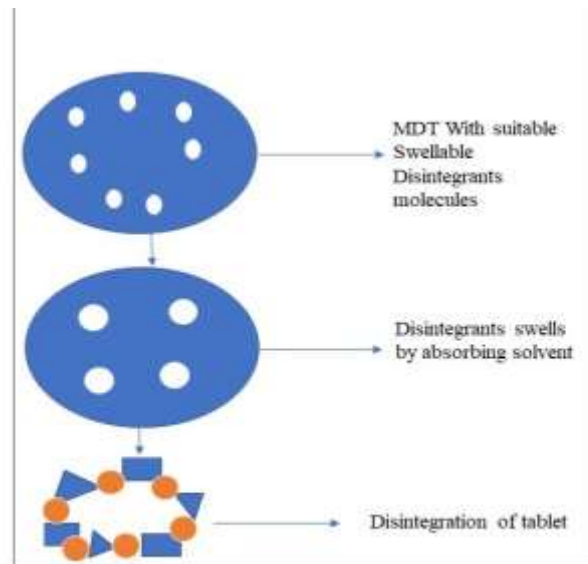


Fig. 4 Swelling activity in tablet disintegration

2. Porosity and Capillary Action (Wicking):
Due to capillary action and porosity, some super disintegrants reveal their characteristics. For example, when crospovidone or croscarmellose tablets are in

touch with a super disintegrant, water seeps into the tablets and causes the rupture of the enter particulate bonus, which causes the tablet to break.



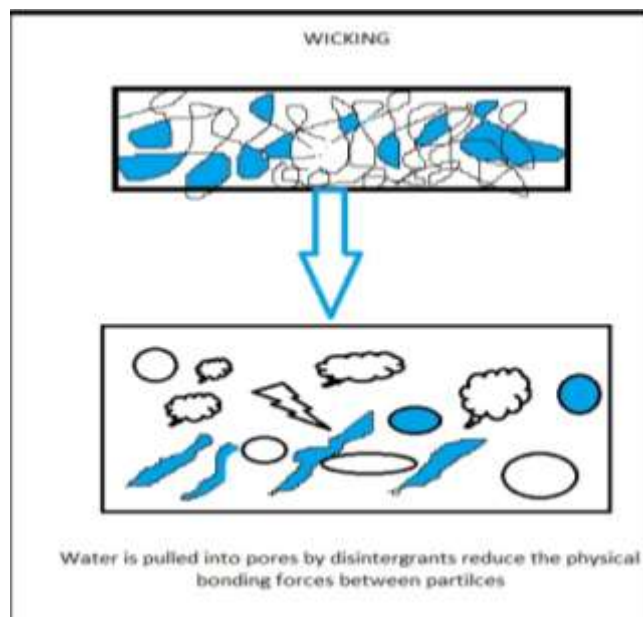


Fig. 5 Wicking

3. Deformation: The word "deformation" refers to a shift in a substance's shape. Due to their plastic nature, super disintegrants attempt to restore their previous shape when force is released after compressing them, which produces deformation.

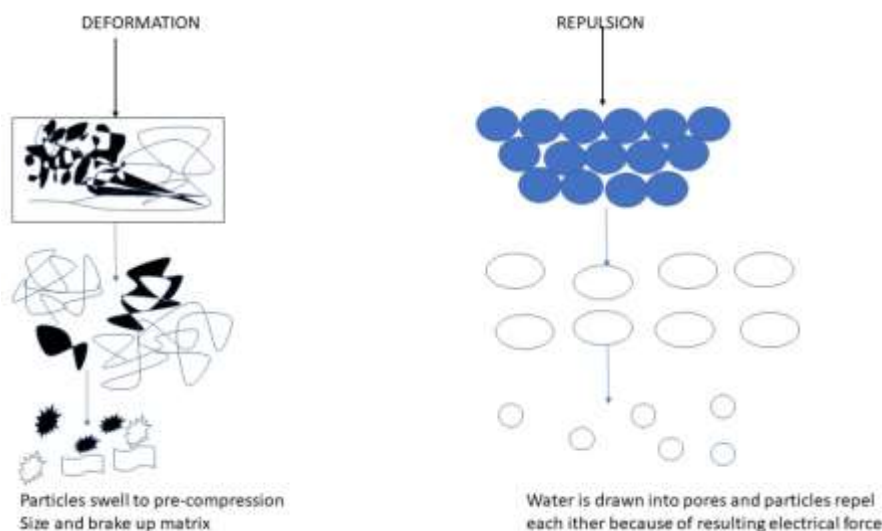


Fig. 6 Deformation and Repulsion

4. Repulsive forces: It is the second mechanism to wicking which is proposed for non-swelling super disintegrant in which electric repulsive forces between particles cause disintegration of the tablets.

5. By Enzymatic Reaction: In this mechanism enzymes in GIT also help in disintegration. These enzymes help by increasing the binding property of the binder to improve disintegration. When super disintegrant swells, it exerts pressure in the outer direction resulting in the burst of the tablet. [24, 25]

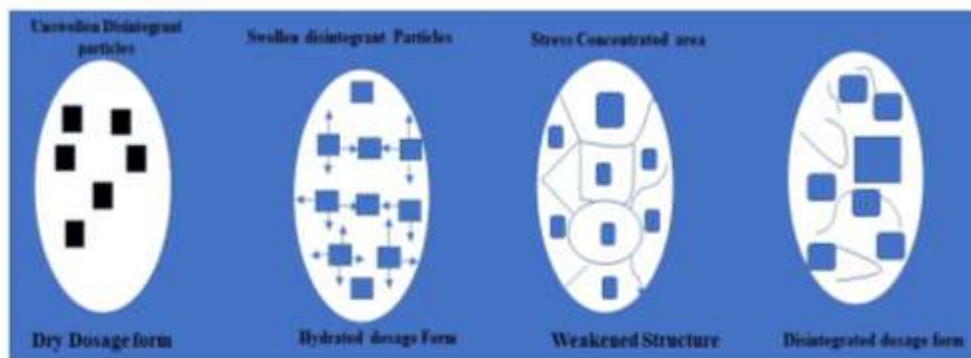


Fig. 7 Enzymes enhance the binding action of binder and help in disintegration
Table 1 List of some super disintegrants with their mechanism of action [26]

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Super disintegrants	Mechanism of action	Special comment	Example
Crospovidone, Kollidon, Polyplasdone	Swells very little and returns to its original size after compression but acts by capillary action	Water is insoluble and spongy so get a porous tablet	Crosslinked PVP
Crosscarmellose, Ac-Di-Sol, Primellose Solutab, Vivasol, L-HPC	Swells 4-8 folds in < 10 seconds. Swelling and wicking both. Swells in two dimensions	Direct compression or Granulation -Starch free	Crosslinked cellulose
Alginic acid, Satialgine	Rapid swelling in an aqueous medium or wicking action	Promote disintegration in both dry and wet granulation	Crosslinked alginic acid
Sodium starch glycolate, Explotab, Primogel	Swells 7-12 folds in < 30 seconds. Swells in three dimensions	high level serve as sustain release matrix	Crosslinked starch
Calcium silicate	Wicking action, Highly porous, Lightweight	The optimum concentration is between 20-40%	Calcium silicate

1.3.6 Some examples of synthetic super disintegrants-

1. Crosscarmellose sodium (CCS)

In little than 10 seconds, CCS may increase by 4–8 times. At low concentrations of 0.5-5.0 percent, swelling and wicking are both the mechanisms by which CCS disintegrates. The cross-linked form of carboxymethyl cellulose

is known as CCS. Numerous studies have demonstrated that CCS has a higher disintegration strength than sodium starch glycolate (SSG).

2. Low-substituted hydroxypropyl cellulose (L-HPC)



It is the go-to super disintegrant for tablets that have been compressed directly and wet granulated. Because of its big particle size, hydroxypropyl exhibits a greater degree of swelling. Researchers like Bi et al. and Watanabe et al. have demonstrated that L-HPC is a superior disintegrant to microcrystalline cellulose.

3. Partially Pregelatinized Starch (PPG Starch)

PPG starch is a type of immediately compressible starch made comprised of whole and partially hydrolyzed ruptured starch granules. However, pregelatinized starch can also be employed as a filler, binder, and disintegrant. PPG starch's effective concentration ranges from 5 to 10%. Swelling is the disintegration's causal mechanism.

4. Cross-linked alginic acid

It is insoluble in water and shows rapid disintegration by swelling or wicking action. It has a high sorption capacity because of its

hydrocolloid nature. Various salt (sodium and potassium) forms of this are used for disintegration.

5. Calcium Silicate

It has a high degree of porosity and is lightweight. It works by wicking action.

6. Ion exchange resins

Indion is a chemical cross-linked polyacrylic polymer. It has a high degree of water uptake. It is a high molecular weight dry powder of weak acid cation exchange resin. It may provide sufficient hardness and chemical stability to the MDTs. The mechanism of action by which it works is swelling.

7. Chitin and Chitosan

The mechanism of action responsible for disintegration is swelling after water uptake for chitin and chitosan when used as super disintegrant. [27]

1.4 TECHNOLOGIES

Table 2 List of Technologies

Technologies for preparing Mouth dissolving Tablets			
S. no.	Conventional Technologies	S. no.	Patented Technologies
1.	Disintegrant Addition	1.	Zydis Technology
2.	Freeze-Drying or Lyophilization	2.	Orasolv Technology
3.	Tablet Moulding	3.	Durasolv Technology
4.	Spray Drying	4.	Wowtab Technology
5.	Sublimation	5.	Flash does Technology
6.	Direct Compression	6.	Flash tab Technology
7.	Mass Extrusion	7.	Oraquick Technology
8.	Cotton Candy Process	8.	Lyoc Technology
9.	Nanonisation	9.	Advatab Technology
10.	Fast Dissolving Film	10.	Dispersible Tablet Technology
		11.	Pharmaburst Technology
		12.	Frosta Technology

1.4.1 Conventional technologies Disintegrant addition



One of the traditional methods is the inclusion of disintegrants. To achieve quick disintegration and a satisfying mouth feel, disintegrant addition should be performed at the highest concentration possible..

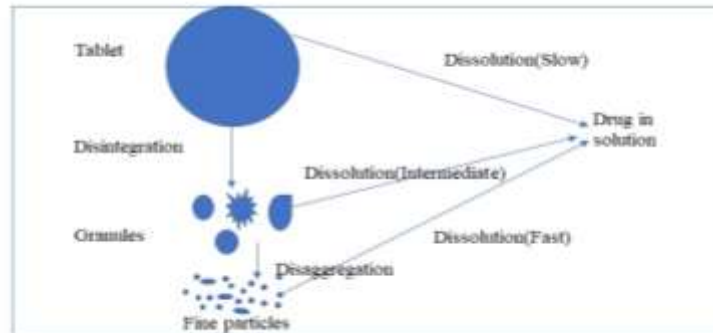


Fig. 8 Disintegrant addition technique

Freeze-drying

One method utilized for the formulation of MDTs is freeze drying because it can lead to the production of a very porous matrix network into tablets, allowing water or saliva to quickly penetrate and dissolve the lyophilized MDT when given to a patient.

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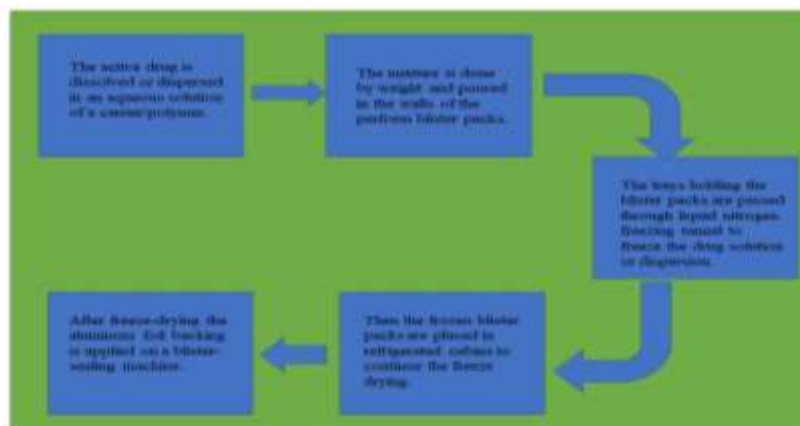


Fig. 9 Steps by step procedure of Lyophilization of MDT

Tablet molding

In this technique, hydrophilic polymers are employed to quickly absorb water, causing the tablet to quickly disintegrate. In this method, a powder mixture is moistened with an appropriate solvent (hydroalcoholic), and

after that, tablets are formed using pressure that is lower than that used in the formulation of a typical tablet. By using hot air, solvent can be removed. Molded tablets have significantly lower mechanical strength than compressed tablets.





Fig. 10 Tablet molding.

Spray drying

Highly porous powders used to create mouth-dissolving tablets are prepared and produced by spray drying. Gelatin, both hydrolyzed and

unhydrolyzed, is added to the formulation as a diluent and a supportive agent. Spray-dried powder for MDTs demonstrated quick dissolution and improved dissolution.

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Fig. 11 Steps involved in Spray Drying Technology

Sublimation

Sublimation of formulated tablets was done to develop a porous matrix by incorporating, volatile ingredients such as camphor.



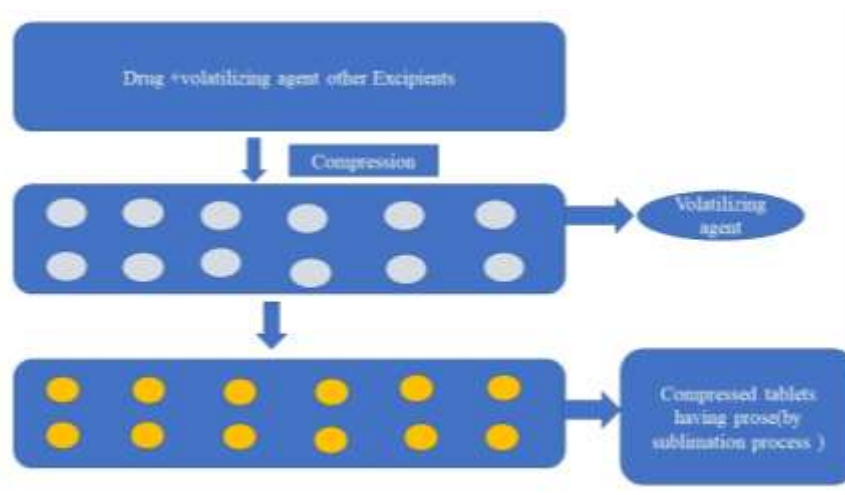


Fig. 12 Steps involved in Sublimation

Table 3 classified sugar-based excipients into two types based on molding and dissolution rate

Type 1	Saccharides (lactose and mannitol)	low mouldability	High dissolution rate
Type 2	Saccharides (maltose and maltitol)	high mouldability	Low dissolution rate

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Nanonization

By using a wet-milling technology, the drug's particle size is reduced to nanoscale in the nanonization process. Surface adsorption on certain stabilizers allows the drug's nanocrystals to be stabilized against agglomeration before being combined into FDTs. This process is especially useful for drugs that don't have enough water solvent. Other advantages of this innovation include speedy dissolution of nanoparticles, which results in increased retention, improved bioavailability, and a reduction in portion, cost-effective manufacturing method, and traditional bundling due of exceptional potency and wide range of dosages (up to 200mg medication per unit).

Fast dissolving films

This method prepares a non-aqueous mixture with water-soluble film-shaping polymer-drugs and other flavor-covering additives that may be used to frame a film once the solvent has been removed. If the drug has an unpleasant taste, resin adsorbate or medication-covered microparticles can be added to the film. When retained in the mouth, this film quickly melts or degrades, releasing the drug in a structure of arrangement or suspension. The most notable aspect of this film is that it can be produced in a variety of sizes, including 22 inches, which may dissolve in 5 seconds to quickly deliver the medication.



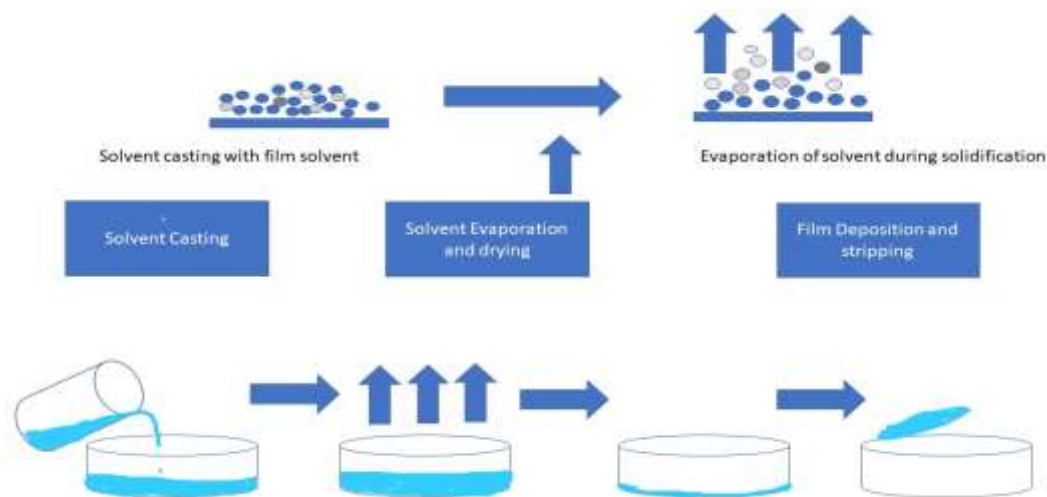


Fig. 14 Fast Dissolving Films Preparation Process [28, 29, 30, 31]

1.4.2 Patented technologies

There are several patented technologies used for developing MDTs; some of them are as:

S.No.	Technology	Technique involved
1	Zydis	This drug is get solubilized within the matrix of the fast-dissolving polymer. When the dosage form is kept in the oral cavity, the freeze-dried matrix breaks rapidly without the aid of water. Several polymers many materials such as Mannitol / Sorbitol, Dextran, Water, Gelatin, various gums, Glycine, etc are used for developing zydis matrix. [32]
2	Orasolv	Orasolv matrix are developed by using effervescent disintegrating agents which are compacted at punching machine at relatively low pressure.[33]
3	Durasolv	Formulation of Durasolvis is similar to OraSolv, despite this containing taste-masked microparticles of a drug, along with drug, fillers, and lubricants. [33]
4	Wow tab	In the Wow tab, sugar-like excipients/Saccharides of both low and high moldability are prepared in the granules. [34]
5	Flash Dose	This system uses the combination of both Shearform and Ceform technologies for the taste masking of the drug. 'Floss' which is a sugar-based matrix, is used to develop this. [34]
6	Flashtab	Coacervation, microencapsulation, simple pan coating methods, and extrusion-spheronisation are used to develop this. [33]
7	Oraquick	Micromask (taste masked microspheres) are used which have enough mechanical strength, and rapid disintegration.
8	Pharmaburst	It utilizes the co-processed excipients to develop MDTs, which dissolve within 30-40 seconds. This technology involves a dry blending of drug, flavor, and lubricant followed by compression into tablets. [35]

9	Frosta	The technology utilizes the conventional wet granulation process and tablet press for the cost-effective production of tablets. The Frosta tablets are mechanically strong with friability of less than 1% and are stable in accelerated stability conditions. Frosta tablets can melt in less than 10 seconds in the oral cavity. [35]
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Orasolv: This technology uses taste-masked APIs and effervescent material, and it is a direct compression method. When a tablet with effervescence comes into touch with saliva or water, the tablet quickly dissolves, leaving coated medication powder behind in less than a minute. It is common practise to employ this method when creating over-the-counter formulations. The Orasolv technology can handle a large variety of APIs, ranging in strength from less than 1 mg to as much as 500 mg. Two dry ingredients make up the effervescent mixture: an effervescent base and an effervescent acid (malic, tartaric, or citric acid) (sodium carbonate, potassium carbonate, potassium bicarbonate). When they come into contact with aqueous liquids, they go through an effervescent process that produces CO₂. This more recent approach creates microparticles by dispersing API into appropriate polymers with other excipients such as mannitol and magnesium oxide. The polymers used for this purpose are ethyl cellulose, methylcellulose, acrylate, and methacrylic acid resins. Tablets developed were fragile and this promoted fast disintegration. To impart physical protection and impermeability to moisture, the tablets were packed in dome-shaped aluminum foil blisters.

Durasolv: It is constructed similarly to Orasolv, but Durasolv is Cima's second-generation formulation for orally disintegrating tablets. The tablets are produced using a lubricant and non-directly compressible fillers (sugars and SAs such as dextrose, mannitol, sorbitol, lactose, and sucrose). The ingredients have a wide surface area due to their tiny particle size, which increases the rate of dissolution. Disintegrants are not used in the formulation, but wicking agents such as carbopol, gums (such as gum arabic and xanthan), and hydroxyalkyl

celluloses (such as hydroxyethylcellulose and hydroxypropylmethylcellulose) are. Due to the use of a higher compaction pressure during tableting, Durasolv has a significantly stronger mechanical strength than Orasolv; as a result, the product can be packaged in either conventional blister packs or vials. NuLev, the most recent Durasolv formulation, is given out in stock bottles. However, When dispensing tablets from stock bottles, caution must be exercised because prolonged exposure to high RH conditions may introduce enough moisture to start the disintegration of the tablet matrix. This method's benefits include low production costs, quick production rates, uniform manufacturing processes, materials, packaging specifications, and low cost and risk dependence. The fact that Durasolv cannot be used for high API dosages is a drawback of the method. The Durasolv technology is appropriate for the formulation of tiny dose tablets of APIs because when the formulation is compressed under high pressure, the patient's taste buds are exposed to the bitter flavour of the medication. The slightly higher price of Durasolv is another drawback longer disintegration time.

Wowtab: Wowtab Tablets are sufficiently hard to maintain the dosage form's physical properties during production and distribution. Saccharides are used in the Wowtab process because they quickly dissolve in water or saliva and compact to the necessary tablet hardness. However, no one saccharide possesses both of these characteristics. They either have quick disintegration characteristics or good compaction hardness. Mannitol, lactose, glucose, sucrose, and erythritol, for instance, were referred to as low moldable sugars because of their features of highly rapid dissolving and poor compressibility. High moldable sugars, such as



maltose, sorbitol, trehalose, and maltitol, exhibit appropriate hardness upon compression, excellent binding, and a slow in vivo disintegration time. The ability of the compound to compress and dissolve rather than the creation of a genuine moulding by solvent wetting and melting is what is meant by the term "moldability." By granulating low and high moldable sugar ratios, a new formulation composition was created. After humidification and drying, the compressed tablet made from the aforementioned formulation demonstrated both quick disintegration and appropriate hardness characteristics. The resulting tablet had a disintegration time of 1–40 s and a hardness of at least 1.0–2.0 kg. Wowtab has a special flavor masking method that gives great tongue feel but smooth melt action.

Flashdose: Fuisz Technologies, a company currently owned by Biovail, developed the flashdose technology (Canada). Three quick-dissolving oral medication delivery devices have been created by Fuisz Technologies. The first two generations of tablets are chewable Soft Chew and EZ Chew varieties that dissolve quickly. Most recently, Fuisz also created Flashdose technology, which creates a cotton candy-like crystal structure using a special spinning mechanism. After incorporating APIs, these crystalline sugars can be crushed into tablets. To cover up the medication's unpleasant taste, flash dose forms combine Ceform™ and the shear form technology. Fuisz has patented the Ceform™ method, which creates homogenous microspheres with an extremely narrow particle size distribution. The matrix was created using a shear form method known as floss, which is created from a number of excipients. Saccharides like sucrose, dextrose, lactose, and fructose make up the floss's cotton candy-like fibers. While other polysaccharides like polymaltodextrins and polydextrose require 30–40% lower temperatures than sucrose, sucrose requires a temperature range of 82–130 °C to be converted into fibers. As a result, it is utilised to incorporate pharmaceuticals that are thermolabile into the formulation. Flashdose created very

porous and hydrophilic tablets due to the relatively low compression pressure used when making the tablets. When in contact with saliva, flash tablets that contain a matrix of sugar fibers quickly dissolve.

Flashtab-The majority of the excipients utilized in this method are those for typical compressed tablets. To create a tablet that dissolves in the mouth in one-minute, coated medication particles are combined with a dissolving agent and a swelling agent. A super disintegrant like crospovidone or croscarmellose and a swelling agent like modified starch or microcrystalline cellulose are both present in a flash tab matrix tablet. The system may also contain a highly water-soluble polyol with binding properties, such as mannitol, sorbitol, maltitol, or xylitol, if no swelling agent is used. Direct coating is used in order to mask the flavor of the active ingredient. The excipients are first granulated using wet or dry granulation in the Flash tab process. They are then combined with coated medication particles and compacted using standard processing machinery to create tablets. High-quality polyvinyl chloride (PVC) or aluminum foils can be used to blister-pack tablets that include hygroscopic ingredients. More moisture is protected by these packing materials than by standard PVC or polypropylene foils.

Oraquick: Oraquick Using patented taste-masking technologies like Flavor and Micro Mask, a formulation was created. KV Pharmaceutical asserts that MicroMask technology provides better taste masking than Flavour-Tech since the medicine is added to the matrix microsphere during the taste-masking process. By dissolving the protein (albumin or gelatin) and sugar (sucrose, mannitol, sorbitol, xylose, dextrose, fructose, or mannose) in an appropriate solvent, such as water, ethanol, isopropyl alcohol, or an ethanol-water mixture, tablets are made using the Oraquick procedure. The matrix solution is then spray-dried to produce granules that are extremely porous. The amount of solvent used during the process determines how porous the final granules are.



After being combined with the medication and any additional tablet excipients or components, these granules are compressed using a low compression pressure. The compressed tablets undergo a sintering step of treatment. Tablets are heated to 90 °C for 10 minutes or sintered in an oven at a temperature of 50 to 100 °C for a few minutes to several hours. Compressing a tablet increases its mechanical strength significantly while maintaining its taste-masking properties.

Lyoc: Lyoc Cephalon Corporation is the owner of the technique. CIMA, a Cephalon subsidiary, presently oversees the R&D activities for Lyoc. This was the first time that a freeze-drying method was employed to create MDTs. Along with APIs, the manufacture of the liquid solution or suspension includes fillers, thickening agents, surfactants, non-volatile flavouring agents, and sweeteners. The uniform liquid that results is put in blister cavities and allowed to freeze-dry. Preservatives are not present in Lyoc pills. The formulation calls for a substantial amount of undissolved inert filler (mannitol) to boost the viscosity of the in-process solution in order to prevent inhomogeneity brought on by sedimentation during this procedure. The high filler content creates denser tablets with disintegration rates similar to those of loosely compressed oral melt formulations by reducing the possible porosity of the dried dosage form. [33, 34]

Advatab: Advatab Based on a proprietary tablet formula created and patent by Kyowa Hakko Kogyo, technology manufactures MDT tablets. During the production process, the lubricant is sprayed onto each tablet individually. The production of conventional tablets involves an internal lubricating system that distributes lubricant on both the inside and the outside of the tablets. The mechanical strength of tablets may be reduced by this technique. Compared to standard tablets, Advatab is made with 10–30 times less hydrophobic lubricant and can be 30–40% stronger. The result is that the pills are robust

and hard but do not prevent liquid entrance when they come into touch with saliva. Advatab can handle coated medication particles and heavy drug loading. Importantly, the technology can be packaged because it doesn't need special packaging in both standard bottles and push-through blisters.

Dispersible Tablet Technology: Lekin Dihydroergotoxin and cimetidine dissolving tablets were patented in Yugoslavia and were said to dissolve in water at room temperature in less than a minute. Water does not readily dissolve dihydroergotoxine in its free basic form. The dissolving rate of dihydroergotoxine methanesulphonate was increased when the organic acid content of dispersible tablets was increased from 0.8 to 10 percent, preferably to 4 percent by weight. A disintegrating agent was one of the crucial excipients used in the cimetidine formulation. It allows for speedy swelling and/or wetting of the pills, which causes them to dissolve quickly. Starch or modified starches, microcrystalline cellulose, alginic acid, cross-linked sodium carboxymethyl cellulose, and cyclodextrin polymers are some of the disintegrating agents. Better disintegration results were obtained when two or more disintegrating agents were used.

Pharmaburst: Pharmaburst Depending on the kind of active component and loading (up to 700 mg), technology uses off-the-shelf processed excipients to generate an MDT that dissolves in 30 to 40 seconds. The amount of Pharmaburst needed in a formulation depends on the tablet's active component. According to the required mouth feel and disintegration time, preliminary trials must be conducted on a formulation by adjusting the amount of Pharmaburst from 50 to 80 percent. A medication, flavour, and lubricant are mixed dry and crushed into tablets using stock tooling on a conventional tablet press. Under standard circumstances for people and temperatures, the production process can be completed. Blister packs or bottles can be used to package the tablets.



Frosta: In order to create robust tablets with high porosity, highly plastic granules are compressed at low pressure using Frosta technology. The highly plastic granules are made up of a binder, a plastic substance that is porous and permeable, and a water penetration enhancer. A fast-melting pharmaceutical tablet can then be created by compressing the highly plastic granules under low pressure. When in contact with water, a porous, plastic substance becomes water soluble or water dispersible, sometimes practically immediately. The likelihood of the interparticle interactions required to create bonds between particles is greatly increased when powders are deformed plastically. The tablets may be delivered in bottles or blister packs. When a polymeric porous and plastic substance dissolves in an aqueous solution, it is crucial to avoid the creation of a viscous layer of the material at the tablet surface. Such tablets can be created, for example, by combining a water penetration enhancer in specific ratios with porous plastic material. In this procedure, water-penetration-improving particles are used to separate the porous and plastic particles, preventing the development of a viscous layer on the tablet surface. The creation of extremely strong bonding among granules at low pressures requires a proper binder, even though porous and plastic materials can generate close contacts to improve the likelihood of joining via compression. [35]

Ceform: This technology calls for the creation of drug-active microspheres. Excipients and drug material are put into a precisely built,

quickly spinning machine, either separately or in conjunction with other pharmaceutical compounds. The dry drug mixture is thrown through the small, heated apertures at a high rate of speed thanks to the action of centrifugal force. The heat from the precisely controlled temperature causes the drug mixture to liquefy to form a sphere without impacting the stability of the medicine. The resulting microspheres are compacted into tablets. The simultaneous processing of the excipients and the medicine results in a special microenvironment where the materials can be integrated into the microspheres, changing their properties such as increasing solubility and stability.

Shearform: A shear form matrix, or "Floss," is constructed using this technology. The feedstock is processed using flash heat after being prepared with a sugar carrier. In this process, sugar experiences both centrifugal force and a temperature gradient at the same time. This causes the mass's temperature to rise, which in turn creates an internal flow condition that allows some of the sugar to move within the mass. Through the rotating head that flings the floss, the flowing mass exits. The floss that is created is amorphous. In order to provide a consistent flow and facilitate mixing, it is further chopped and recrystallized using a variety of processes. The active ingredient, other excipients, and recrystallized matrix are then combined before being crushed into tablets. It is possible to mix active medications and other excipients with the floss before recrystallizing it. [36]

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Table 4 Marketed formulation of MDTs [37]

Trade name	Active drug	Manufacturer
Felden fast melt	Piroxicam	Pfizer Inc., NY, USA
Claritin Redi Tab	Loratidine	Schering plough corp., USA
Maxalt MLT	Rizatripten	Merck and Co., NJ, USA
Zyprexa	Olanzapine	Eli Lilly, Indianapolis, USA
Nimulid MDT	Nimesulide	Panacea Biotech, New Delhi, India
Torrox MT	Rofecoxib	Torrent pharmaceuticals, India
Romilast	Montelukast	Ranbaxy lab. Ltd. New Delhi, India



Stemetil MD	Prochlorperazine maleate	Abbott Pvt. Ltd. Baddi, Solan HP.
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Conclusion- To create more pleasing properties including color, texture, tongue feel, and flavor muffling, film and sugar coatings are a crucial component of the tablet's formulation. Film and sugar coatings have a number of drawbacks, but the most significant is that the use of aqueous or organic solvents results in toxicity. The Tablet in Tablet method is the greatest workaround for the aforementioned issue. The Tablet in Tablet approach can be used to create modified release systems for pharmaceuticals that are comparable to one another or for drugs that belong to distinct categories, or to release drugs at separate sites for absorption. Tablets are a flexible dosage form that combine the benefits of solid products' stability and manufacturability with favorable organoleptic and administration characteristics. There are more opportunities for the use of chewable tablets in specific populations like pediatrics and differentiated pharmaceutical products as well as in other healthcare markets like nutritional products, nutraceuticals, and veterinary medicines as a result of the increased focus on patient-centric formulations in drug delivery.

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