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REVIEW OF FAST DISSOLVING TABLET

Ms. Rutuja .V. Yadav[1], Mr. Ketan .S. Jadhav[2],Mr. Aftab .S. Amte[3], Ms. Shilpa .S. Gawade[4], Dr. Pravin Kumar Sable[5]

S.S.P.SHIKSHAN SANSTHA,SIDDHI COLLEGE OF PHARMACY,CHIKHALI PUNE-411062

ABSTRACT

Fast dissolving tablets have gained popularity, particularly among pediatric and geriatric patients who have conditions like Parkinson's disorder or hand tremors. Capsules and tablets face challenges such as dysphagia, which can lead to non-compliance and ineffective therapy. However, oral dosage forms are still preferred for drug administration. Fast dissolving tablets dissolve quickly in saliva without the need for water, offering a convenient dosing option. They are designed to disintegrate rapidly in the mouth, containing super disintegrates to aid the process. These tablets provide advantages such as easy portability, accurate dosing, stability, and suitability for both geriatric and pediatric patients. The rapid disintegration and absorption of fast dissolving tablets result in improved drug release time and enhanced bioavailability, making them valuable in pharmaceuticals. This article explores the importance of non-invasive drug delivery systems in meeting the needs of the pharmaceutical industry, aiming to enhance drug half-life, solubility/stability, and bioavailability, among other factors.

Keywords: Fast Dissolving Tablet, Fast Dissolving Dosage Form, Challenges in formulation, Techniques of FDT, Various Technologies, Superdisintegrants.

Introduction [1-6]

Oral drug delivery is the preferred method for administering various medications due to its ease, accuracy, and patient compliance. However, the challenge lies in swallowing solid dosage forms like tablets and capsules, especially for certain patient populations and those with specific lifestyle constraints. To address this issue, orally dispersible tablets that rapidly dissolve in the oral cavity have been developed. These tablets are not only beneficial for individuals with swallowing difficulties but also for active individuals who require convenient medication options. Recent advancements in novel drug delivery systems focus on improving the safety and efficacy of drug molecules by creating dosage forms that enhance patient compliance. Fast-dissolving drug-delivery systems have emerged as an alternative to traditional solid-dosage forms, particularly for pediatric and geriatric patients. The rapid solubility of drugs in these systems leads to quicker absorption and onset of clinical effects. Orally disintegrating tablet technology has gained recognition in the industry and academia, with the USFDA defining it as a solid dosage form that disintegrates rapidly for efficient drug delivery.

Orally disintegrating tablets are also called as Orodispersible tablets, forms as ODTs[7]

- **Quick disintegrating tablets,**
- **Mouth dissolving tablets,**
- **Fast disintegrating tablets,**
- **Fast dissolving tablets,**
- **Rapid dissolving tablets,**
- **Porous tablets,**
- **Rapid melts.**

Among the terms mentioned above, the dosage approved by the United States Pharmacopeia (USP) stands out.

2] Criteria for FDT [8,9]

- Fast dissolving tablets (FDTs) do not need water to be swallowed and should dissolve or disintegrate in the mouth within a few seconds.

- FDTs can accommodate high drug loading.
- FDTs provide a pleasant mouth feel.
- After oral administration, FDTs leave minimal or no residue in the mouth.
- They should require a lower dose.
- FDTs are composed of small to lower molecule weight.
- They are partially non-ionized in the oral cavity at pH 6.8.
- FDTs are free from a bitter taste.
- They exhibit low sensitivity to environmental conditions such as humidity and temperature.
- FDTs allow the manufacturing of tablets using conventional processing and packaging equipment at a low cost.

3] Need for development of FDT [9]

A) Patient Factors

Fast dissolving dosage forms are ideal for patients who have difficulty swallowing traditional tablets and capsules, such as pediatric and geriatric patients. Examples include elderly patients with depression, middle-aged patients undergoing radiation therapy for breast cancer, schizophrenic patients attempting to conceal tablets, and patients experiencing persistent nausea.

B) Effectiveness Factor

Salivary dispersion in the oral cavity leads to drug absorption before reaching the stomach, enhancing dissolution. This pre-gastric absorption bypasses initial liver metabolism, boosting bioavailability. Additionally, drugs prone to generating harmful metabolites through first-pass liver and gastric metabolism may have enhanced safety profiles.

C) Manufacturing and Marketing Factors

Pharmaceutical manufacturers often create new and enhanced dosage forms for drugs approaching the end of their patent life in order to prolong market exclusivity, enhance product distinctiveness, and extend patent protection.

(4) Advantages of Fast Dissolving Tablets [5, 10]

- Water is not needed for administration, making it convenient for patients.
- Provides a pleasant mouth feel and is cost-effective.
- Offers a quicker onset of action compared to traditional dosage forms.
- Easy to administer for patients who have difficulty swallowing tablets.
- Has a high drug loading capacity and improved bioavailability.
- Enhances bioavailability by allowing drug absorption before reaching the stomach.
- Can be formulated to dissolve without leaving residue in the mouth, ensuring a pleasant experience.
- Resistant to environmental factors like temperature and humidity.
- Exhibits good stability, ease of handling, precise dosing, and simple manufacturing.
- FDT can mask unpleasant odors and bitter tastes.
- Useful in managing sudden allergic reactions and motion sickness.
- Supports product promotion, line extension, and patent life extension.
- Compatible with existing packaging and processing equipment.

5] Limitations of Fast Dissolving Tablets [5, 10]

- Adequate mechanical strength is often lacking in tablets, necessitating cautious handling.
- Improper formulation of tablets can result in an unpleasant taste and/or gritty sensation in the mouth.
- Formulating drugs with high doses into Fast Dissolving Tablets (FDTs) poses challenges.

6] Challenges in formulation of fast dissolving tablets [1, 11, 12]

1) Mechanical strength and disintegration time:

Enhancing the mechanical strength inevitably prolongs the disintegration time, making it crucial to strike a balance between these two factors. Formulating FDTs aims to achieve disintegration times typically under one minute, while simultaneously addressing the challenge of maintaining satisfactory mechanical strength.

2) Taste masking:

Rapid disintegrating drug delivery systems often include the medication in a taste masked form due to the unpleasant taste of most drugs. These delivery systems dissolve or disintegrate in the patient's mouth, allowing the active ingredients to come into contact with the taste buds. Therefore, ensuring that the drugs are taste-masked is crucial for patient compliance.

3) Aqueous solubility:

Water-soluble drugs present formulation challenges due to the formation of eutectic mixtures, leading to a decrease in freezing point and the creation of a glassy solid that may collapse when dried due to the loss of structural support during sublimation. To prevent this collapse, matrix-forming excipients like mannitol can be used to induce crystallinity and provide rigidity to the amorphous composite.

4) Hygroscopicity:

The moisture-absorbing nature of a powder, known as hygroscopicity, is an important characteristic. In the case of a powder with high solubility, its hygroscopicity is closely linked to its solubility. However, it is crucial for Fast Dissolving Tablets (FDTs) to have low sensitivity to humidity. This can be challenging due to the use of highly water-soluble excipients in the formulation, which are prone to moisture absorption and may even dissolve completely in high humidity. To safeguard FDTs from different environmental conditions, it is essential to develop effective packaging or implement other protective strategies.

5) Amount of drug:

The utilization of FDT technologies is constrained by the quantity of drug that can be included in each unit dose. In the case of lyophilized dosage forms, the drug dosage should not exceed 400 mg for insoluble drugs and 60 mg for soluble drugs. This factor poses a significant challenge in the formulation of fast-dissolving oral films.

6) Size of tablet:

Studies have shown that tablets measuring 7-8 mm are the easiest to swallow, while those larger than 8 mm are easier to handle. Consequently, finding a tablet size that is both easy to swallow

and easy to handle poses a challenge.

7) Mouth feel:

It is important that FDTs do not break down into larger particles in the mouth. The particles that are produced after the FDTs disintegrate should be as tiny as possible. Additionally, the inclusion of flavors and cooling agents such as menthol enhances the sensation in the mouth.

8) Sensitivity to environmental conditions:

It is essential for FDTs to demonstrate minimal sensitivity to environmental factors like humidity and temperature, given that the majority of materials utilized in FDTs are designed to dissolve in minimal water content.

7] Techniques for Preparing Fast Dissolving Tablets [13,14,15]

Numerous methods have been documented for the development of Fast dissolving tablets or Oro dispersible tablets. In this discussion, we will explore the primary techniques that are commonly employed in formulating these tablets.

1. Freeze drying/ Lyophilisation
2. Tablet molding
3. Spray drying
4. Direct Compression
5. Sublimation
6. Mass Extrusion
7. Cotton Candy Process
8. Phase transition process
9. Nanonization
10. Effervescent agent addition method

- **Freeze-Drying or Lyophillisation**

The product undergoes freeze drying, a process where water is removed through sublimation after freezing. This method results in a porous structure that can dissolve quickly. A standard procedure

for manufacturing FDT using freeze drying is outlined. It has been shown that this technique enhances absorption and bioavailability. However, the drawbacks of lyophilization include its high cost and time-consuming nature.

- **Tablet Molding**

There are two types of molding processes: solvent method and heat method. Tablets made using the solvent method have a less compact structure compared to compressed tablets, resulting in a porous structure that aids in faster dissolution. To enhance the mechanical strength of the tablets, binding agents are required. However, taste masking poses an additional challenge in this technology. To address this, the drug particles are concealed by spray congealing a molten mixture of hydrogenated polyethylene glycol, cottonseed oil, lecithin, and sodium carbonate, which is then incorporated into a lactose-based tablet triturate form. In terms of scalability for industrial manufacturing, the molding technique is easier to scale up compared to the lyophilization technique.

- **Spray Drying**:

Gelatin serves as a matrix and supporting agent, mannitol as a bulking agent, and super disintegrates such as croscarmellose, sodium starch glycolate, or crospovidone in this method. Tablets made from spray dried powder with bulking agent, super disintegrate, and acidic (citric acid) and/or alkaline (sodium bicarbonate) ingredients have been observed to disintegrate in less than 20 seconds in water.

- **Sublimation:**

Volatile components are added to create a porous mixture, which undergoes sublimation to remove the volatile material, resulting in a porous matrix. Common volatile ingredients such as benzoic acid, ammonium bicarbonate, and urea are compressed into tablets with other excipients. Tablets produced using this method typically disintegrate in 10-20 seconds, thanks to the highly porous structure left behind after sublimation. Solvents like benzene and cyclohexane can also be utilized as pore-forming agents in this process.

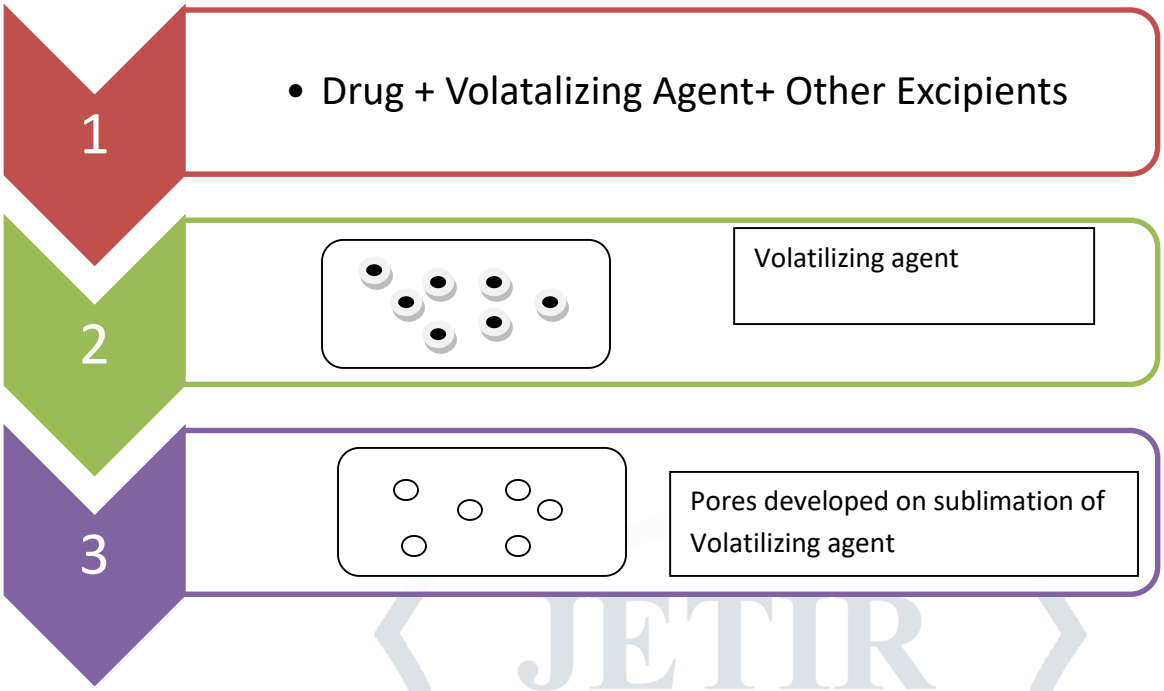

Fig. 2 Sublimation Method

- **Direct Compression:**

The simplest and most cost-effective method for manufacturing tablets is direct compression. With the availability of advanced excipients like super disintegrants and sugar-based excipients, this technique can now be used to prepare Fast Dissolving Tablets.

- **Mass-Extrusion:**

The active blend in this technology is softened by a solvent mixture of water-soluble methanol and polyethylene glycol. The softened mass is then expelled through an extruder or syringe to form a cylinder product, which is divided into even segments using a heated blade to create tablets. Additionally, the dried cylinder can be utilized to coat granules for bitter drugs, effectively achieving taste masking.

- **Cotton Candy Process:**

The technique used in this process is called spinning, which creates a crystalline structure similar to cotton candy. The process involves melting and spinning polysaccharides or saccharides to form a matrix, which is then partially recrystallized for better flow properties and compressibility. This matrix is then mixed with active ingredients and excipients, compressed into orally

disintegrating tablets (ODT), and can handle high drug doses while providing enhanced mechanical strength. However, the high temperature involved in the process restricts its use.

- **Phase transition process**

The degradation of orally disintegrating tablets (ODT) was examined through the phase transition of sugar alcohols such as erythritol, xylitol, trehalose, and mannitol. Tablets were manufactured by compacting a powder containing two sugar alcohols with varying melting points and then heating them within the range of their respective melting points. Prior to the heating step, the tablets lacked sufficient hardness due to poor compatibility. However, post-heating, the tablet hardness increased as a result of enhanced inter-particle bonds or increased bonding surface area induced by the phase transition of the sugar alcohol with the lower melting point.

- **Nanonization**

Nano melt technology has been developed for drugs with poor water solubility. This method involves reducing the particle size to the Nano scale through wet milling. The drug's Nano crystals are prevented from clumping together by incorporating stabilizers into FDTs through surface adsorption. As a result, absorption and bioavailability are enhanced, and the required dose can be reduced. This technique is applicable to a wide range of doses, including drug doses of up to 200mg per unit.

8] Patented Technologies for Fast Dissolving Tablets: [13, 14, 16, 17, 18, 19]

1) Zydis Technology

The Zydis formulation is a unique technology used to create fast dissolving tablets. Unlike traditional tablets, Zydis tablets are freeze dried and contain drug materials that are either physically trapped or dissolved within a matrix of fast dissolving carrier materials. One of the advantages of Zydis tablets is that they do not require water for swallowing. When the Zydis unit is placed in the mouth, the freeze dried structure quickly disintegrates. The composition of Zydis material includes various substances that serve different purposes. Polymers like dextran, alginate, and gelatin are added to provide strength during handling. Saccharides such as sorbitol or mannitol are incorporated to enhance elegance, hardness, and crystallinity. Glycine is commonly used as a collapse protectant to prevent shrinkage of the Zydis unit during freeze

drying or long-term storage. To protect the formulation from moisture, it is recommended to pack Zydis tablets in a blister packaging.

2) Durasolv Technology:

CIMA labs has developed a patented technology called Durasolv, which is used to create tablets. These tablets are composed of a drug, filler, and a lubricant. They are made using standard tableting equipment and have excellent rigidity. Additionally, they can be easily packaged in conventional blister packaging. Durasolv is particularly suitable for products that require small quantities of active ingredients.

3) Orasolv Technology

CIMA LAB introduced the innovative Orasolv technology, which is an effervescent direct compression tablet designed to dissolve quickly in the mouth with minimal effervescence, leaving behind a coated drug powder to mask the drug's taste. However, a drawback of Orasolv is its reduced mechanical strength caused by light compression.

4) Wow Technology

Yamanouchi Pharmaceutical Corporation holds the patent for a process known as "wow," which stands for "without water." This method involves combining high mold ability saccharide, such as oligosaccharide and mannitol, with low mold ability saccharides like glucose, lactose, and mannitol to produce a quickly dissolving, sturdy tablet.

5) Shearform Technology:

The foundation of this technology lies in the preparation of floss, which involves subjecting a feed stock containing sugar carrier to a flash heat process. A mixture of sucrose with either mannitol or dextrose, along with a surfactant, is well blended to create the primary floss mixture. During the flash heat process, the carrier materials experience an internal flow condition induced by heat, exiting through a spinning head while the floss is flung under centrifugal force. The resulting floss consists of longer fibers, which are then chopped into smaller particles using a high shear mixer granulator. Recrystallization is achieved through ethanol treatment (1%), followed by spraying out the floss, subsequent evaporation, enhancing flow and cohesive properties. The

recrystallized matrix is then combined with drugs and other excipients before undergoing compression to produce tablets that are porous, have a pleasant mouth feel, and rapidly dissolve upon contact with saliva.

6) Flash dose Technology:

The technology employed in this process is similar to that of cotton candy, utilizing a distinct spinning mechanism to create a crystalline floss structure. By incorporating the drug into this crystalline sugar and compressing it into a tablet, a product with a large surface area for quick dissolution and easy dispersion on the tongue is achieved. These Flash dose tablets are composed of a self-binding shear form matrix known as "floss".

7) Ceform Technology:

The key element of this procedure involves loading a dry powder mixture of pure drug and excipients into a high-speed rotating machine. The centrifugal force generated by the spinning head of the ceform machine mixes the dry drug powder rapidly through a small heated opening. The resulting drug blend is melted into spherical microspheres due to controlled temperature microbursts, without compromising drug stability. These microspheres are then either blended or compressed into the predetermined oral dosage form.

8) Flash tab Technology:

The Flash tab technology, developed by Prographarm laboratories, has been patented. This innovative tablet system incorporates active ingredients in the form of micro crystals. The production of drug micro granules can be achieved through various conventional techniques such as coacervation, micro encapsulation, and extrusion spheronisation. Throughout the manufacturing process, conventional tableting technology is employed.

- **Nanocrystal Technology:**

The dissolution rate is improved through the reduction of particle size and the increase in surface area, thanks to technology. Drug particles known as nano-crystal particles, which have a diameter of less than 1000 nm, are created by milling the drug substance. This Nano crystal fast dissolving technology offers a wide range of doses per unit, with the potential to contain up to 200 mg of

API per unit. It also enhances the pharmacokinetics of oral drugs and allows for the use of non-moisture sensitive actives. Additionally, it is both cost-effective and economically viable.

- **Advantol 200:**

Advantol 200 is an excipient system designed specifically for Nutraceutical applications. It offers the unique feature of "Soft-Melt" functionality, allowing for the production of easily compressible tablets. The advantage of Advantol 200 is that it does not require any specialized manufacturing equipment or tooling. By using a standard rotary tablet press with standard tooling, and operating under normal tableting temperature and humidity conditions, robust "soft melt" tablets can be effortlessly produced.

- **Advatab:**

AdvaTab™ technology, developed and patented by Kyowa Hakko Kogyo in Tokyo, Japan, creates orally dissolving tablets with a unique composition that is well lubricated through a spray process during production. These tablets require 10–30 times less hydrophobic lubricant compared to traditional tablets, making them 30–40% stronger while still maintaining easy wetting upon contact with saliva for improved mouth feel. AdvaTab™ tablets do not need special packaging and can be conveniently packed in standard packaging systems like push-through blisters and bottles.

- **Frosta Technology:**

The core of this technology involves the creation of sturdy tablets with high porosity by compressing highly plastic granules at low pressures to form rapidly dissolving tablets. These granules can be categorized into three components: a porous and plastic material, a water penetration enhancer, and a binder. The porous, plastic material is either water-soluble or water-dispersible, and plastic deformations of powders improve inter-particle contacts crucial for bonding between particles. If the porous and plastic material is polymeric, it is important to prevent the formation of a viscous layer on the tablet surface when it comes into contact with aqueous media. One method of producing such tablets is by blending the porous, plastic material with a water penetration enhancer at specific ratios to avoid the formation of a viscous layer on

the tablet surface. This results in Fast Dissolving Tablets (FDTs) with the desired hardness and disintegration time ranging from 2 to 30 seconds, depending on the tablet size.

- **Ora-Quick Technology:**

KV Pharmaceutical asserts that its microsphere technology, named Micro Mask, employs a distinctive patented taste masking method without the use of solvents, resulting in faster and more efficient tablet manufacturing. Additionally, it boasts lower heat generation, making it ideal for drugs sensitive to temperature changes. This technology promises improved taste masking and quicker dissolution of tablets. No other products utilizing this technology, except those from KV Pharmaceuticals, are currently on the market. The technology assesses various parameters including absorption and dissolution rates, mouth feel, taste, strength, bioavailability, and stability.

- **Pharmaburst Technology:**

The technology patented by SPI Pharma in New Castle involves the use of coprocessor excipients that dissolve within 30-40 seconds. This innovative method includes dry blending the drug, flavor, and lubricant before compressing them into tablets. The resulting tablets are strong enough to be packaged in blister packs and bottles.

Drugproduct	Activeingredient	Indication	Marketing company	Technology	Technology Company
Alavert	Loratadine	Allergy	Wyeth	OraSolv/DuraSolv	Cima Lab
Aricept	Donepezil	Alzheimers	Eisai		
Benadryl Fast	Diphenhydramine pseudoephedrine	Allergy, cold, sinus	Johnson & Johnson	WOWTAB	Astellaspharma
Claritin RediTabs	Loratadine	Allergy	Schering-Plough	Zydis	Cardinal Health
PrevacidSoluTab	Lansoprazole	Duodenal ulcer	TAP		
RemeronSolTab	Mirtazapine	Depression	Organon	Durasolv	Cima Lab
Maxalt-MLD	Rizatriptan benzoate	Migrane	Merck	Zydis	Cardinal Health

Table.1Commercially Available Patented Fast Dissolving Technologies

9] Formulation and Development of Fast Disintegrating Tablets [18,19,37,38,39]

Essential components in the development of FDTs must facilitate rapid drug release for accelerated dissolution, encompassing both active ingredients and excipients. The disintegration and solubilization of a directly compressed tablet rely on the synergistic actions of disintegrants, water-soluble excipients, and effervescent agents. Common excipients found in FDTs typically include a disintegrant, a diluent, a lubricant, and optionally sweeteners and flavoring agents. Optimal bulk excipients for orally disintegrating formulations should possess specific characteristics,

1. The residue-free dispersion occurs within seconds.
2. It effectively masks the unpleasant taste of the drug and provides a pleasing sensation in the mouth.
3. It allows for adequate drug loading and maintains stability even in varying humidity and temperature conditions. Excipients play a crucial role in tablet formulation. Detail of excipients is given in table

Excipients	Function	Examples
Superdisintegrant	Increases the rate of disintegration and hence the dissolution. The presence of other formulation ingredients such as water-soluble excipients and effervescent agents further hastens the process of disintegration. For the success of fast dissolving tablet, the tablet having quick dissolving property which is achieved by using the super disintegrant	Crospovidone, Microcrystalline cellulose, sodium starch glycolate, sodium carboxy methyl cellulose, pregelatinzed starch, Carboxy methyl cellulose, and modified corn starch. Sodium starch glycolate has good flowability than crosscarmellose sodium. Cross povidone is fibrous nature and highly compactable
Flavors	Increases Patient compliance and acceptability	Peppermint flavor, cooling flavor, flavor oils and flavoring aromatic oil, peppermint oil, clove oil, bay oil, anise oil, eucalyptus oil thyme oil, oil of bitter

		almonds. Flavoring agents include, vanilla, citrus oils, fruit essences.
Sweeteners and sugar based excipients	This is another approach to manufacture ODT by direct compression. Sugar based excipients acts as bulking agents .These exhibits high aqueous solubility and sweetness, and hence impart taste masking property and a pleasing mouth feel.	Artificial sweeteners like Aspartame, Sugars derivatives. Bulking agents like dextrose, fructose, isomalt, lactilol, maltitol, maltose, mannitol, sorbitol, starch hydrolysate, polydextrose and xylitol
Surface Active agents	Reduces interfacial tension and thus enhances solubilization of FDT	(Spans), polyoxyethylene stearates.Sodiumdoecylsulfate, sodiumlaurylsulfate, polyoxyethylene sorbitan fatty acid esters (Tweens), sorbitan fatty acid esters
Binder	Maintains integrity of dosage form prior to	Polyvinylpyrrolidone(PVP),Polyvinylalcohl(PVA)

	administration	Hydroxy propyl methylcellulose(HPMC)
Color	Enhances appearance and organoleptic properties of dosage form	Sunset yellow, Amaranth, Red iron oxide
Lubricants	Lubricant helps reduce friction and wear by introducing a lubricating film between mechanical moving parts of tablet punching machine	Stearic acid, Magnesium stearates, Zinc state, calcium state, talc, polyethylene glycol, liquid paraffin, magnesium lauryl sulfate, colloidal silicon dioxide.
Fillers	Enhances bulk of dosage form	Directly compressible spray dried Mannitol, Sorbitol, xylitol, calcium carbonate, magnesium carbonate, calcium phosphate, calcium sulfate, pregelatinzed starch, magnesium trisilicate, aluminium hydroxide

Table.2 Excepients used in preparation of fast dissolving tablets

10] Super Disintegrants [20, 21, 22, 23]

Super disintegrants are essential for the development of Fast Dissolving Tablets (FDTs) as they facilitate rapid disintegration and dissolution through swelling and water absorption. The swelling

of super disintegrants increases the wetted surface of the carrier, improving wet ability and dispensability, thereby enhancing disintegration and dissolution. The optimal concentration of super disintegrants should be chosen based on the critical concentration required for disintegration, as tablet disintegration time is affected by the concentration of super disintegrants.

10.1] Mechanism of action of disintegrants

A. By capillary action

The initial stage is always disintegration through capillary action. Once the tablet is placed in a suitable liquid, the liquid enters the tablet and displaces the air that was adsorbed on the particles. This process weakens the bonds between the molecules and causes the tablet to break into smaller particles. The amount of water absorbed by the tablet depends on the drug/excipient's hydrophilicity and the conditions under which the tablet was made. In order for these types of disintegrants to work effectively, it is important to maintain a porous structure and have a low interfacial tension with the liquid, which helps create a hydrophilic network around the drug particles.

B. By swelling

Tablet disintegration is commonly understood to occur through swelling, with tablets that have high porosity experiencing poor disintegration due to insufficient swelling force. Conversely, tablets with low porosity exert enough swelling force. It is important to mention that when the packing fraction is extremely high, fluid cannot penetrate the tablet, resulting in a slowdown of disintegration.

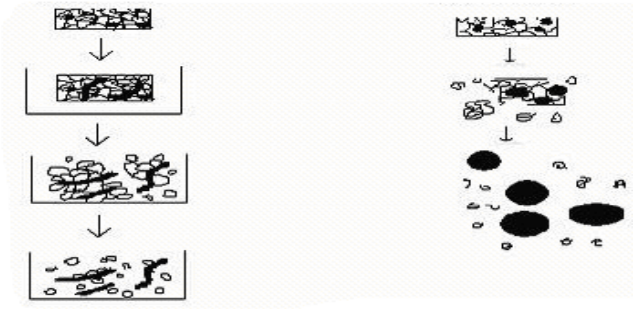

Fig.3Mechanism of Superdisintegrants- wicking & swelling Porosity

WICKING

SWELLINGG

C. Due to disintegrating particle/particle repulsive forces

One alternative explanation for the swelling of tablets made with 'non-swellable' disintegrants is the particle repulsion theory proposed by Guyot-Hermann. This theory suggests that even non-swelling particles can contribute to the disintegration of tablets due to electric repulsive forces between particles. However, it is important to note that water is still required for this mechanism to occur. Researchers have discovered that repulsion is actually secondary to wicking.

D. Because of Heat of Wetting (Air Expansion)

Disintegrants with exothermic properties create localized stress when wetted, leading to capillary air expansion that aids in tablet disintegration. However, this explanation is applicable to only select disintegrants and does not encompass the action of many modern disintegrating agents.

E. Due to deformation

Hess demonstrated that disintegrated particles undergo deformation during tablet compression, and these deformed particles regain their original structure upon contact with water or aqueous media. In some cases, the swelling capacity of starch was found to be enhanced when granules experienced significant deformation during compression.

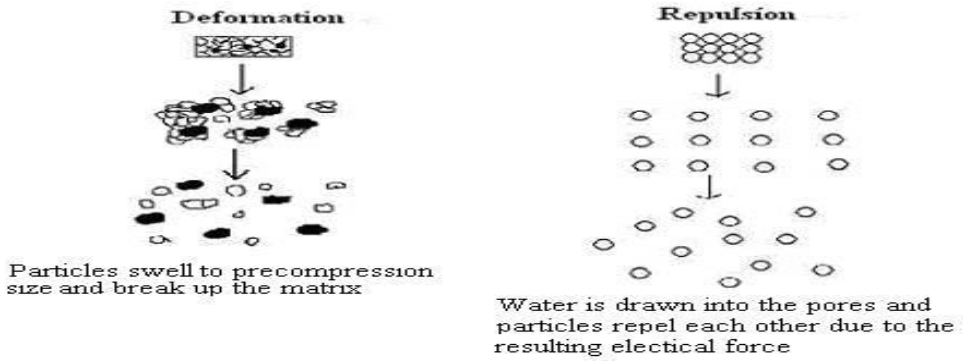

Fig. 4 Mechanism of Superdisintegrants Deformation and particle-particle repulsive forces

F] Due to Release of Gases

When a tablet gets wet, carbon dioxide is released because of the interaction between bicarbonate and carbonate with citric acid or tartaric acid. This causes the tablet to break down due to the pressure generated inside it. Pharmacists use effervescent mixtures when they need to create tablets that dissolve very quickly. However, these disintegrants are sensitive to even slight changes in humidity and temperature, so strict control of the manufacturing environment is necessary. The effervescent blend can be added either right before compression or in two separate parts of the formulation.

G] By Enzymatic Reaction

Enzymes found in the body function as disintegrants, breaking down the binding properties of binders to aid in disintegration.

10.2] Types of Superdisintegrants:

The Superdisintegrants can be classified:

- Natural Superdisintegrants
- Synthetic Superdisintegrants

- **Natural Superdisintegrants:**

Superdisintegrating agents of natural origin are preferred over synthetic substances due to their cost-effectiveness, abundant availability, non-irritating and non-toxic nature. Natural materials like gums and mucilage's have been extensively utilized in drug delivery for their easy availability, eco-friendliness, emollient and non-irritating properties, non-toxicity, ability for chemical modifications, potential degradability, and compatibility due to their natural origin. Various gums and mucilage's, such as Plant ago Ovate husk, Locust Bean gum, Treated agar, Plant ago Ovate mucilage, Plant ago Ovate seed powder, and Cassia fistula gum, exhibit super-disintegrating activity.

2. Synthetic Superdisintegrants:

Superdisintegrants such as croscarmellose sodium (Ac-Di-Sol), sodium starch glycolate (Primo

eland Exploitable), and crosspovidone (Polyplasdone XL) are effective in addressing these issues. The use of Superdisintegrants in fast dispersible tablets is feasible as it ensures optimal physical properties of the tablet. For instance, the combination of crosspovidone, croscarmellose sodium, and sodium starch glycolate, along with other sublimating agents like camphor and ammonium bicarbonate, can be utilized to enhance the disintegration of the tablet.

Superdisintegrants	Commercially available grades	Mechanism of action	Special comment
Crosslinked cellulose	Croscarmellose® Ac-Di-Sol®, NymceZSX®, Primellose®,	Swells 4-8 folds in <10seconds Swelling and wicking both.	Swells in two dimensionsDirect compression or Granulation Starch free.
Crosslinked PVP	CrosspovidonM® Kollidon® Polyplasdone	Swells very little and returns to original size aftercompression but act by capillary action.	Water insoluble and spongy in nature so get porous tablet.
Crosslinked starch	Explotab® Primogel®	Swells 7-12 folds in < 30 seconds.	Swells in three dimensions and high Level serves as sustain release matrix.
Crosslinked alginicacid	Alginic acid NF	Rapid swelling in aqueous medium or wicking action.	Promote disintegration in both dry or wet granulation
Soy polysaccharides	Emcosoy®	Rapid Dissolving	Used in nutritional products.
Crosslinked polymer of Polycarboxylic acids	Kyron T-314	High swelling tendency of Hydration. Swelling Index 12	Elimination of lump formation. It is suitable for the both wet granulation as well as

Table.3 Examples of Superdisintegrants

10.3] Selection Criteria for Superdisintegrants [27, 28]

While superdisintegrants mainly impact the disintegration rate, their effects can extend beyond that. High levels of superdisintegrants can also influence the mouth feel, tablet hardness, and friability. Therefore, it is crucial to consider several ideal factors when choosing the right superdisintegrant for a specific formulation:

1. Proceed for rapid disintegration, when tablet comes in contact with water.
2. Be compactable enough to produce less friable tablets.
3. Produce good mouth feel to the patients. Thus, small particle size is preferred to achieve patient compliance.
4. Have good flow, since it improves the flow characteristics of total blend.

11] Preformulation studies fast dissolving tablet [10, 24, 25, 26]

1) Bulk Density (Db):

The bulk density of a powder is determined by measuring the initial weight of powder poured into a measuring cylinder after passing through a standard sieve #20. This weight represents the bulk volume, and the bulk density is then calculated using the provided formula. The bulk density is expressed in grams per milliliter (g/ml). To calculate the bulk density of a powder, the initial weight of the powder (which has passed through a standard sieve #20) is measured by pouring it into a measuring cylinder. This initial volume is known as the bulk volume, and the bulk density is determined using the given formula. The bulk density is expressed in grams per milliliter (g/ml).

Db = M/ Vb

Where, M is the mass of powder

Vb is the bulk volume of the powder.

2) Tapped Density (Dt):

The powder's bulk density is determined by the ratio of its total mass to the tapped volume, which is measured by tapping the powder either 750 times or 1250 times until the difference between successive volumes is less than 2% in a bulk density apparatus. The bulk density is expressed in g/ml and is calculated using the formula: total mass of the powder / tapped volume of the powder.

Dt = M / Vt

Where, M is the mass of powder

Vt is the tapped volume of the powder.

3) Angle of Repose (θ):

The angle of repose (θ) is a measure of the friction forces present in loose powder, indicating its flow properties. It represents the maximum angle between the surface of the powder pile and the horizontal plane.

$$\tan(\theta) = h / r$$

$$\theta = \tan^{-1}(h / r)$$

Where, θ is the angle of repose.

h is the height in cms

r is the radius in cms.

Sr. No.	Angle of Repose (°)	Type of Flow
1	< 20	Excellent
2	20 – 30	Good
3	30 – 34	Passable
4	> 34	Very Poor

Table.4 Angle of Repose as an Indication of Powder Flow Properties

4) Carr's index (or) % compressibility:

Powder flow properties are indicated by a percentage value, which is provided as a measure.

$$I = \frac{D_t - D_b}{D_t} \times 100$$

Where, Dt is the tapped density of the powder and

Db is the bulk density of the powder.

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

Table.5 Relationship between % compressibility and flow ability

5) Hausner ratio:

The Hausner ratio serves as an indirect measure of powder flowability. Its calculation involves the use of the following formula.

$$\text{Hausner ratio} = \frac{D_t}{D_b}$$

Where, Dt is the tapped density.

Db is the bulk density.

Lower hausner ratio (<1.25) indicates better flow properties than higher ones (>1.25).

12] EVALUATION FAST DISSOLVING TABLET [27-36]

1) General Appearance : The overall look of a tablet, including its visual appeal and perceived elegance, plays a crucial role in consumer approval. Factors such as size, shape, color, presence or absence of odor, taste, surface texture, physical imperfections, consistency, and legibility of any identifying marks are all important considerations.

2) Size and Shape: The dimensions and form of the tablet can be accurately defined, supervised, and regulated.

3) Tablet thickness: The thickness of tablets plays a crucial role in replicating their appearance and facilitating accurate counting with filling equipment. Certain filling machines rely on the consistent thickness of tablets for precise counting. A total of ten tablets were selected and measured using a micrometer to record their thickness.

4) Weight variation: A total of 20 tablets were randomly chosen from the batch and individually weighed to assess weight differences. The weight deviation criteria according to the I.P. standards are outlined in the table below.

Average Weight of Tablet	% Deviation
80 mg or less	±10
80 mg to 250 mg	±7.5
250 mg or more	±5

Table.6 Average Weight of Tablet

5) Hardness: The manufacturing of DTs requires specialized processes and ingredients, making it challenging to achieve a significant strength. To ensure early disintegration in the mouth, the hardness limit of the tablets is typically kept low. The tablet's hardness can be measured using a conventional hardness test.

6) Friability: Formulators face a challenge in achieving the desired friability percentage for DTs due to the manufacturing methods that tend to increase friability values. Therefore, it is crucial to evaluate this parameter and ensure that the results fall within the specified limits of 0.1-0.9%.

7) Wetting time and water absorption ratio: The wetting time of a dosage form is influenced by the contact angle, while the wetting time of the DTs is an important parameter that provides insights into the tablet's disintegration properties. A lower wetting time indicates a faster disintegration of the tablet. To measure the wetting time of the tablets, a simple procedure can be followed. Five circular tissue papers with a diameter of 10cm are placed in a petri dish, and 10 milliliters of a water-soluble dye solution is added. The tablet is carefully placed on the surface of the tissue paper, and the time it takes for the water to reach the upper surface of the tablet is recorded as the wetting time. To determine the water absorption ratio, the weight of the tablet before placing it in the petri dish (Wb) is noted. After the tablet is wetted in the petri dish, it is taken out and reweighed (Wa). The water absorption ratio (R) can be calculated using the following equation.

$$R = 100\ (Wa\text{-}Wb) / Wb$$

8) Disintegration test: DTs typically disintegrate in less than one minute, but patients may experience disintegration times ranging from 5 to 30 seconds. The current standard procedure for testing disintegration in these dosage forms has limitations and cannot accurately measure very short disintegration times. To properly assess the disintegration of DTs, the test should simulate the process that occurs in the mouth with the presence of saliva.

9) Dissolution test: The approach to developing dissolution methods for DTs is similar to that of conventional tablets, unless taste masking is not used. In such cases, the drugs may have

dissolution conditions as stated in the USP monograph. Other media, such as 0.1 N HCl, pH 4.5, and pH 6.8 buffers, should be used to evaluate DTs in the same way as regular tablets. The USP 2 paddle apparatus, with a paddle speed of 50 rpm, is commonly used for dissolution testing of DT tablets. However, slower paddle speeds can be used to obtain a comparative profile, especially when the dissolution of DTs is very fast under USP monograph conditions. When dealing with large DT tablets that weigh around or exceed one gram and contain dense particles, using higher paddle speeds can prevent the formation of a mound in the dissolution vessel. This allows for a suitable range of stirring speeds between 25-75 rpm. The USP 1 (basket) apparatus is less commonly used for DTs due to specific physical properties of the tablets. Tablet fragments or disintegration tablet masses may get trapped on the inside top of the basket at the spindle, where effective stirring does not occur. This can lead to inconsistent results in the dissolution profile.

10) Stability testing of drug (temperature dependent stability studies):

The fast-dissolving tablets are carefully packaged and stored under specific conditions as recommended by ICH guidelines for accelerated studies.

(1) 40 ± 1 °C (2) 50 ± 1°c (3) 37 ±1 ° C and RH 75% ± 5%

The tablets underwent analysis for physical characteristics such as visual defects, hardness, friability, disintegrations, dissolution, and drug content after being withdrawn for a period of 15 days. The obtained data was then fitted into first-order equations to determine the degradation kinetics. Additionally, accelerated stability data was plotted according to the Arrhenius equation to determine the shelf life at 25°C.

- **Drug content determination:**

Three randomly selected uncoated tablets were used to determine their average weight. The tablets were crushed and a precise amount of the resulting powder was taken. This powder was then transferred to three 100 ml volumetric flasks and diluted with phosphate buffer solution (pH 6.8) up to the mark. The flasks were periodically shaken and left for 24 hours to ensure complete solvation of the drug. The mixtures were filtered, appropriately diluted, and the absorbances were measured at λ max nm against a blank reference. The drug content in each tablet was determined using the standard calibration curve of the drug in phosphate buffer pH 6.8 solution.

CONCLUSION

The development and acceptance of Fast Dissolving Tablets (FDTs) signify a significant advancement in oral drug delivery. The rapid action observed with FDTs is largely attributed to the anatomical and physiological characteristics of the buccal cavity, which play a crucial role in facilitating drug absorption through the buccal mucosa.Drugs are absorbed rapidly through the buccal mucosa due to the unique characteristics of the buccal cavity, leading to fast-acting effects with Fast Dissolving Tablets (FDTs). FDTs offer advantages like simple administration, precise dosing, and rapid absorption, but formulation challenges need to be overcome to maximize their benefits for improving patient compliance and therapeutic outcomes.

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