Deep Freeze-Dried Orally Disintegrating Tablets (ODTs) for Thermolabile APIs

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Abstract: Lyophilised orally disintegrating tablets (ODTs) have achieved a great success in overcoming dysphagia associated with conventional solid dosage forms. However, the extensive use of saccharides within the formulation limits their use in treatment of chronic illnesses. The current study demonstrates the feasibility of using combination of proline and serine to formulate zero sacharide ODTs and investigates the effect of freezing protocol on sublimation rate and tablets characteristics. The results showed that inclusion of proline and serine improved ODT properties when compared to individual counterparts. Additionally, annealing the ODTs facilitated the sublimation process and shortened the disintegration time. Lyophilised orally disintegrating tablets (ODTs) have achieved a great success in overcoming dysphagia associated with conventional solid dosage forms. However, the extensive use of saccharides within the formulation limits their use in treatment of chronic illnesses. The current study demonstrates the feasibility of using combination of proline and serine to formulate zero sacharide ODTs and investigates the effect of freezing protocol on sublimation rate and tablets characteristics. The results showed that inclusion of proline and serine improved ODT properties when compared to individual counterparts. Additionally, annealing the ODTs facilitated the sublimation process and shortened the disintegration time. The pharmaceutical industry's demand for fast disintegration tablets (FDTs) has grown over the last few years, and the field is growing quickly. Fast dissolving tablets (FDTs) are solid dosages that dissolve rapidly on the tongue and absorb the drug with the need for water in a few seconds. FDTs have been developed for bedridden, elderly, and paediatric patients as well as active individuals who are on the go and may not having access to water. Due to hand tremors and dysphasia, many older people will have trouble swallowing traditional oral dosage forms, including tablets, capsules, and solution suspensions. There is the opportunity to expand the product line with this composition. The appropriateness of drug applications, Super-disintegrants working and other technology created for FDTs, in addition to assessment methods and other items that are advertised.

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Keywords

Fast Disintegration Tablet (FDT), Solid Dosage Form, Super Disintegrates, Bioavailability

Introduction

Development of solid oral dosage forms that disintegrate/dissolve rapidly in the mouth when in contact with saliva has attracted substantial attention in both academia and industry in order to address swallowing difficulties (dysphagia) associated with the conventional solid oral dosage forms (tablets and capsules) experienced by wide range of patient population [1]. These formulations are commonly referred to as orally disintegrating tablets (ODTs), orodispersible tablets, fast dissolving tablets, fast dispersing tablets, rapid dissolving tablets or fast melting tablets (FMTs).

ODTs offer many advantages over other solid oral dosage forms. They can be easily swallowed (in contrast to conventional tablets and hard gelatin capsules) and can be used with patients who have difficulty in swallowing such as stroke victims, psychiatric, pediatric and geriatric patients [2]. ODTs also need no preparatory step prior to administration and therefore preferable when compared to extemporaneous suspension or effervescent granules. They have pleasant mouth feel and acceptable taste [3] and are preferred over the chewable tablets in which the bitter drug may leach during mastication [4]. Additionally, ODTs can be designed to provide fast onset of action by enhancing pre-gastric absorption through the buccal cavity, pharynx and oesophagus [2,5], and to increase the bioavailability by incorporating emulsions within the tablets [6,7].

Of the plethora of technologies available to fabricate ODTs such as three dimensional printing, moulding and direct compression, lyophilisation has been considered the most successful, as the resultant tablets have a highly porous structure, which permits rapid disintegration and hence easy swallowing. However one of the major drawbacks associated with freeze dried ODTs is the extensive use of saccharides and polyols in the formulation which limits there use in the treatment of chronic medical conditions and also for multiple dose

medications primarily due to the limited allowable daily intake of these saccharides and polyols especially in pediatric, diabetic and obese patients.
Research from our laboratory investigating the feasibility of using individual amino acids as matrix supporting/ disintegration enhancer agents in the formulation of lyophilised orally disintegrating tablets (data not published), has shown varied capability of amino acids to fulfill all the required characteristics for the formulation of lyophilised ODTs. For instance, proline showed complete wettability in water (disintegrating medium) with short wetting time, which is expected to improve the disintegration of ODTs; however, its inclusion in freeze dried formulations was limited due to the extremely low glass transition temperatures and consequently resulting in the collapse of the prepared formulations. On the other hand, serine based formulations displayed higher collapse temperature and produced elegant tablets even at high concentration, due to its tendency to crystallise in the frozen state, but was characterised by long disintegration time, which was explained by serine's partial wetting property, as the measured contact angel (θ) with water was $0^o < \theta < 90^o$.

Oral drug delivery remains the most preferred and convenient route of administration due to its simplicity, non-invasiveness, patient compliance, and cost-effectiveness. Among the various oral dosage forms, tablets are widely accepted because of their stability, accuracy in dosage, ease of administration, and portability. However, conventional tablets pose challenges for specific patient populations, such as pediatric, geriatric, and mentally ill patients, who often face difficulty swallowing solid oral dosage forms [1]. To address this limitation, **Fast Disintegrating Tablets (FDTs),** also known as **orally disintegrating tablets (ODTs)** or **mouth-dissolving tablets (MDTs),** have emerged as a novel and patient-friendly dosage form.
Fast disintegrating tablets are solid unit dosage forms that disintegrate or dissolve rapidly (generally within 30 seconds to 3 minutes) in the mouth without the need for water, releasing the active pharmaceutical ingredient (API) for immediate absorption. This unique feature enhances the bioavailability of drugs, particularly those subjected to first-pass metabolism, and improves the onset of therapeutic action. The development of FDTs has significantly transformed the pharmaceutical landscape by combining the advantages of solid and liquid dosage forms, especially for medications used in emergency conditions such as allergic reactions, epilepsy, or cardiac pain [2,3].
The formulation of FDTs involves careful selection and optimization of excipients such as superdisintegrants, fillers, binders, and flavoring agents. Superdisintegrants like crospovidone, sodium starch glycolate, and croscarmellose sodium are primarily responsible for the rapid disintegration of the tablet in saliva. Additionally, the incorporation of taste-masking agents, sweeteners, and saliva-stimulating agents further enhances patient acceptability and compliance. Various techniques are employed in the manufacture of FDTs, including direct compression, sublimation, spray drying, lyophilization (freeze-drying), and molding. Each method has its own advantages and limitations in terms of cost, stability, mechanical strength, and ease of scaling up. A thorough understanding of the physicochemical properties of the drug and excipients is crucial for selecting the appropriate formulation strategy.
Evaluation of fast disintegrating tablets involves a series of pre-compression and post-compression parameters such as flow properties of powder blends, hardness, friability, weight variation, disintegration time, wetting time, drug content uniformity, and in vitro dissolution. These tests ensure the quality, efficacy, and reproducibility of the final product. This comprehensive review aims to provide an in-depth overview of the formulation aspects, excipient selection, manufacturing techniques, and evaluation parameters associated with fast disintegrating tablets. It also highlights the challenges and future prospects in the development of FDTs as an effective and patient-centric drug delivery system [4].

ADVANTAGES OF FAST DISINTEGRATING TABLETS (FDTs)

1. **Rapid Disintegration Time**
   - The tablet should disintegrate within 30 seconds or less in the oral cavity without the need for water.
   - Quick disintegration enhances drug dissolution and absorption for faster onset of action.
2. **Pleasant Taste and Mouthfeel**
   - FDTs must have a palatable taste and smooth mouthfeel to ensure patient compliance.
   - Use of sweeteners, flavoring agents, and taste-masking techniques is essential to avoid bitterness.
3. **Sufficient Mechanical Strength and Hardness**

- Tablets must be strong enough to withstand handling, packaging, and transportation.
- Despite their porous nature, they should not crumble or break easily during normal handling.

4. **Low Friability**
   - FDTs should not chip or powder easily.
   - Low friability is essential to ensure tablet integrity throughout its shelf life.
5. **Uniform Drug Content**
   - Each tablet should contain a consistent and accurate amount of the active pharmaceutical ingredient (API).
   - Content uniformity is crucial, especially for low-dose drugs.
6. **Good Stability**
   - FDTs must remain stable in terms of physical integrity, disintegration properties, and drug content over their shelf life.
   - Due to their hygroscopic nature, proper packaging (e.g., aluminum blisters) is necessary to protect them from moisture.
7. **Wide API Compatibility**
   - The formulation should be compatible with various types of APIs, including those with poor solubility or sensitivity to moisture.
   - It should maintain the drug's stability and bioavailability after disintegration.
8. **Cost-Effective and Scalable Manufacturing**
   - The formulation process should be economical and suitable for large-scale production.
   - Techniques like direct compression, melt granulation, and spray drying are preferred for ease and reproducibility.
9. **Water-Free Administration**
   - FDTs must be easily administered without the need for water.
   - This is especially beneficial for pediatric, geriatric, bedridden, and mentally ill patients who have difficulty swallowing.
10. **Patient Compliance and Acceptability**
    - The formulation must be designed to enhance patient comfort and willingness to use the medication.
    - This includes minimal residue in the mouth and no choking hazard [5].

DISADVANTAGES OF FAST DISINTEGRATING TABLETS (FDTs)

1. **Limited Stability**
   - FDTs are more prone to moisture absorption due to their porous nature. This can lead to degradation of the active ingredients or changes in the tablet's physical properties.
   - Special packaging (e.g., moisture-resistant blister packs) is required to maintain stability, which can increase production costs.
2. **Low Mechanical Strength**
   - FDTs tend to be fragile due to their low density and high porosity.
   - They can break or crumble easily during handling, packaging, or transport, leading to potential dosing inaccuracies or product loss.
3. **Short Shelf Life**
   - The hygroscopic nature of FDTs makes them susceptible to moisture-related degradation, which can reduce their shelf life.
   - In addition, prolonged exposure to air or light may affect the drug's stability and efficacy.
4. **Limited Load of Active Pharmaceutical Ingredients (APIs)**
   - FDTs are generally suitable for low to medium-dose drugs.
   - For drugs that require a high dose, the tablet size can become impractically large, affecting patient compliance and manufacturability.
5. **Possible Residue or Aftertaste**
   - Although taste-masking techniques are used, some FDTs may leave a residue in the mouth or cause an unpleasant aftertaste.
   - This can negatively impact patient acceptability, especially in formulations that are not adequately masked for bitter drugs.
6. **Risk of Cross-Contamination**

- The high porosity and quick disintegration of FDTs mean that handling and storing multiple tablet types can result in the risk of cross-contamination between different formulations.
- This requires extra precautions during manufacturing and packaging.

7. **Limited Formulation Options for Certain Drugs**
   - FDTs are not suitable for all drug types. Drugs that are unstable in moisture, heat-sensitive, or require slow release may not be ideal candidates for FDT formulations.
   - Some APIs may also require specific excipient combinations or specialized manufacturing techniques, limiting the scope of drug compatibility [6].

MECHANISM OF DISINTEGRATION OF FAST DISINTEGRATING TABLETS (FDTs)

The disintegration of Fast Disintegrating Tablets (FDTs) is governed by several physicochemical processes that are primarily driven by the nature of the formulation, particularly the superdisintegrants used. The main mechanisms involved in tablet disintegration include swelling, wicking, deformation recovery, heat of wetting, enzymatic action, effervescence, and, in many cases, a combination of these mechanisms.

Swelling is one of the most fundamental and widely utilized mechanisms in the design of FDTs. When the tablet comes into contact with saliva, certain superdisintegrants rapidly absorb water and swell significantly. This expansion increases the internal pressure within the tablet matrix, which ultimately causes the tablet to break apart into smaller fragments. Superdisintegrants such as sodium starch glycolate (SSG) and croscarmellose sodium (CCS) are highly effective due to their strong swelling properties. The efficiency of this mechanism is influenced by the particle size, cross-linking degree, and surface area of the disintegrant used.

Wicking, also known as capillary action, plays a vital role in the rapid disintegration of porous FDTs. This mechanism involves the penetration of saliva into the pores of the tablet, which occurs as a result of capillary forces. As the liquid moves into the pores, it displaces air, resulting in wetting of the tablet structure. This rapid fluid uptake weakens the physical bonding between particles, leading to the breakdown of the tablet. Crospovidone is a key example of a superdisintegrant that works predominantly through the wicking mechanism due to its highly porous nature and hydrophilicity.

Deformation recovery is another important mechanism, particularly relevant during the compression phase of tablet manufacturing. Some disintegrants become deformed under high compression forces but possess the ability to recover their original shape upon contact with water. This elastic recovery creates mechanical stress within the tablet, which contributes to its rapid break-up. Crospovidone again serves as a notable example, demonstrating a dual mechanism both wicking and deformation recovery for efficient disintegration.

Heat of wetting is a lesser-known but still significant mechanism in certain formulations. Some excipients, upon contact with water, undergo an exothermic wetting reaction, releasing heat. This localized rise in temperature can accelerate the absorption of water and contribute to the disruption of the tablet matrix. Although not a dominant disintegration pathway, the heat of wetting can enhance the overall disintegration process when used alongside swelling or wicking agents.

Enzymatic action is particularly relevant in formulations containing natural polymers or starch-based excipients. Saliva contains enzymes such as amylase that can hydrolyze polysaccharides like starch. The enzymatic degradation of such materials weakens the matrix structure and promotes disintegration. This mechanism is especially useful in herbal and nutraceutical tablets, where natural excipients are commonly employed.

Effervescence is a chemically driven disintegration mechanism that involves a reaction between a weak acid (e.g., citric acid) and a carbonate or bicarbonate (e.g., sodium bicarbonate) in the presence of water. The reaction produces carbon dioxide gas, which builds internal pressure and causes the tablet to burst apart. This method provides very fast disintegration and is often accompanied by a refreshing mouthfeel. However, effervescent FDTs require moisture-resistant packaging due to their sensitivity to environmental humidity.

Combination mechanisms are commonly employed in modern FDT formulations. Rarely does a single mechanism operate in isolation; instead, formulators often use a strategic blend of superdisintegrants to exploit multiple disintegration pathways. For example, combining crospovidone (which acts through wicking and deformation recovery) with sodium starch glycolate (which acts through swelling) results in synergistic effects, ensuring rapid and efficient tablet disintegration. The combination approach offers flexibility in

formulation design and enhances performance across a variety of active pharmaceutical ingredients [7-11].

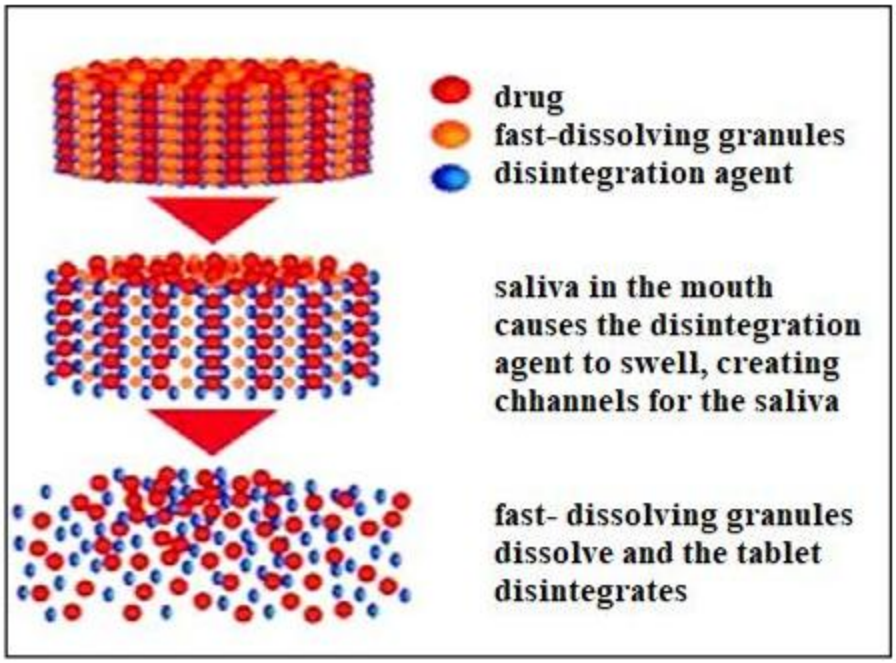

Figure 1: Mechanism of Disintegration of FDT

SUPERDISINTEGRANTS IN FAST DISINTEGRATING TABLETS (FDTs)

Superdisintegrants are crucial excipients used in the formulation of Fast Disintegrating Tablets (FDTs) to facilitate rapid disintegration and dissolution. These substances are highly efficient at promoting the breakdown of the tablet matrix upon contact with water or saliva, allowing the tablet to disintegrate quickly in the oral cavity. The effectiveness of a superdisintegrant is determined by its ability to swell, absorb water, and promote the breakup of the tablet into smaller particles, leading to faster release of the active pharmaceutical ingredient (API) [12].

Types of Superdisintegrants

There are several types of superdisintegrants, each with distinct mechanisms of action and characteristics. The choice of superdisintegrant is dependent on the specific drug formulation, the required disintegration time, and the desired release profile of the tablet.

Starch Derivatives Starch-based superdisintegrants, such as sodium starch glycolate (SSG) and pregelatinized starch, are widely used in FDT formulations. These excipients are known for their excellent swelling properties, which cause the tablet to break apart when it absorbs water. Sodium starch glycolate, in particular, is effective due to its ability to swell and expand upon water uptake, exerting mechanical stress on the tablet matrix, leading to disintegration. These superdisintegrants are biodegradable and well-tolerated, making them suitable for both pharmaceutical and nutraceutical applications.

Cellulose Derivatives Another popular class of superdisintegrants includes cellulose-based compounds such as croscarmellose sodium (CCS) and crospovidone. These materials exhibit both swelling and wicking properties, where the liquid is drawn into the tablet matrix through capillary action, causing it to break apart. Croscarmellose sodium is highly effective due to its ability to rapidly absorb water and swell, while crospovidone works by both absorbing water and exerting elastic forces upon wetting. These superdisintegrants are particularly useful in formulations that require fast disintegration in the oral cavity.

Effervescent Agents Effervescent agents, such as sodium bicarbonate and citric acid, are commonly used in conjunction with other superdisintegrants in FDTs. These agents react with water to release carbon dioxide gas, which creates pressure within the tablet, causing it to break apart quickly. The effervescence not only aids in disintegration but also enhances the dissolution rate of the API by increasing the surface area exposed to the dissolving medium. This mechanism is particularly useful in formulations that require a very rapid onset of action.

Synthetic Superdisintegrants Synthetic superdisintegrants, such as cross-linked polyvinylpyrrolidone (crospovidone) and cross-linked carboxymethylcellulose (cross-linked CMC), are also widely used due to their superior disintegration properties. These excipients are highly efficient at absorbing water and causing rapid tablet breakdown. Crospovidone, for example, is highly effective due to its swelling capacity and the formation of a gel-like structure upon water absorption, which helps disrupt the tablet matrix. Cross-linked CMC works similarly, swelling upon hydration and breaking apart the tablet efficiently. These superdisintegrants are commonly used in a wide range of pharmaceutical formulations due to their high efficiency and reproducibility.

Other Natural Polymers Other natural polymers, such as guar gum and xanthan gum, have also been explored as superdisintegrants. These polysaccharides are particularly valuable in formulations targeting specific drug release profiles. Guar gum is known for its ability to swell significantly in water, while xanthan gum exhibits both swelling and gel-forming properties. These polymers may be used in combination with other excipients to enhance disintegration and improve overall tablet performance.

Factors Influencing the Selection of Superdisintegrants

- **Type of Active Pharmaceutical Ingredient (API)**: Some APIs may require specific superdisintegrants that work best with their solubility or stability profiles.
- **Disintegration Time**: Different superdisintegrants contribute varying disintegration times, with some providing faster disintegration than others.
- **Compatibility with Other Excipients**: It is crucial to ensure that the selected superdisintegrant does not interact negatively with other components of the tablet formulation, such as binders, fillers, or lubricants.
- **Cost and Availability**: While synthetic superdisintegrants may offer superior performance, natural alternatives may be more cost-effective and suitable for large-scale manufacturing.
- **Toxicity and Biocompatibility**: The selected superdisintegrant should be biocompatible and non-toxic to ensure the safety of the final dosage form, especially for drugs intended for long-term use [12-15].

TECHNOLOGIES AND EVALUATION

Technologies used to get ready for rdt13 a variety of methods, which are described below, are frequently used to create rapidly dissolving systems. These consist of mass extrusion, sublimation, or spray drying, direct compression, molding, and freeze-drying or lyophilization.

1. Freeze-drying

The technique of freeze-drying, also known as lyophilization, involves sublimating water that has been removed from a frozen product. The primary benefit is that pharmaceutical materials can be produced at low temperatures, which eliminates harmful thermal effects, and maintained in a dry form with comparatively minimal stability issues over the course of their shelf life. Compared to other solid products on the market, freeze-dried versions offer faster rates of disintegration. By giving the bulking agents and occasionally the medication a glassy amorphous structure, the lyophilization process improves the formulation's dissolving properties. The application of freeze-drying is severely limited, though, due to the handling and time needed for the process, the small number of materials handled in batches, and the costly expenses of the equipment and processing.

2. Disintegrant addition

The disintegrant addition process is popular for making fast-disintegrating tablets due to its inexpensive and simple to utilize. When creating rapid-dissolving tablets using the disintegrant addition approach, the fundamental idea is to add super disintegrants in the right amounts to promote both a pleasant mouthfeel and quick disintegration.

3. Moulding

The moulding process involves either The drug solution can be made by evaporating the solvent, suspending it at room pressure (without vacuum the lyophilization), or When moulding the moist mixture into tablets (compression molding, which uses less force than conventional tablet compression), it is dissolved, moistened, or dispersed with a solvent. compression-molded tablets are allowed to air dry. The molded tablet has a very porous structure due to the decreased compression force used compared to traditional tablets, which speeds up the product's dissolution and disintegration. To speed up the product's dissolving rate, however, the powder mixture must be sieved with a very fine screen. Tablet disintegration and mouthfeel are enhanced by the molding procedure, which is commonly used with substances that are soluble (saccharides) Nevertheless, the low mechanical strength of molded tablets causes erosion and fracture when handled. Tablets that dissolve in the mouth can be made using a variety of molding techniques.

a. **Compression Moulding** The powder combination is broken down into mold plates to create a wetted mass after being previously wetted in a solvent, such as ethanol/water.
b. **Heat Moulding** Mouth-dispersing tablets can be made directly from a molten substance in which the medication dissolves or disperses.
c. **No Vacuums** Lyophilisation in this procedure, a solvent is evaporated from a medication suspension or solution at a constant pressure.

4. Sublimation

The limited porosity of the tablets is the reason why even highly water-soluble components in compressed tablets dissolve slowly. Other tablet ingredients were combined with inert solids that volatilize easily, such as camphor, ammonium bicarbonate, urea, ammonium carbonate, and hexa methelene tetramine, and the mixture was compacted into tablets. The volatile components were subsequently removed by sublimation, which produced porous structures. According to claims, tablets produced using this method often disintegrate in 10–20 seconds. As agents that create pores, solvents like benzene and cyclohexane can be used.

5. Spray drying

Spray drying can produce thin, rapidly dissolving powders that are incredibly porous. As auxiliary materials, both hydrolyzed or non-hydrolyzed gelatins are utilized in the bulking ingredient mannitol, the disintegration agent sodium substance to improve dissolution and disintegration. The compacted tablet made from After 20 seconds of immersion in an aqueous solution, the spray-dried powder dissolved.

6. Mass extrusion

In order to create tablets, this method softens the active blend with a solvent mixture of methanol and polyethylene glycol soluble in water, and the expulsion of softened bulk using an syringe or extruder that uses a heated blade to split the product a cylinder into uniform segments. Drug granules with a bitter flavor can also be coated with the dried cylinder to cover up the bitterness.

7. Direct compression

The direct compression process is the easiest method to produce tablets and FMTs. Direct compression has the major benefit of being inexpensive to produce. It uses common equipment, a limited number of steps, and readily available excipients. 2 Large doses can also be employed in FMTs, as the final weight of them frequently exceeds that of the manufacturing process. Disintegrants, effervescent agents, and water-soluble excipients can be used singly or in combination to break down and dissolve the direct compression tablet. The disintegration time is generally acceptable, although the number of tablets and hardness have a significant (and constrained) impact on the dissolving efficacy. It is possible for large, hard pills to disintegrate. Longer than needed for FMTs in most cases. Because of this, goods with the best disintegration qualities frequently having a medium to small weights and/or poor physical resistance (minimum hardness and high friability). Inadequate physical resistance causes tablet rupture during the blister alveolus's opening, hazardous powder to be present during the blistering stage, and tablet edges to break during handling. For FMTs created via direct compression, the disintegrants frequently are important to the disintegration and dissolution process [16].

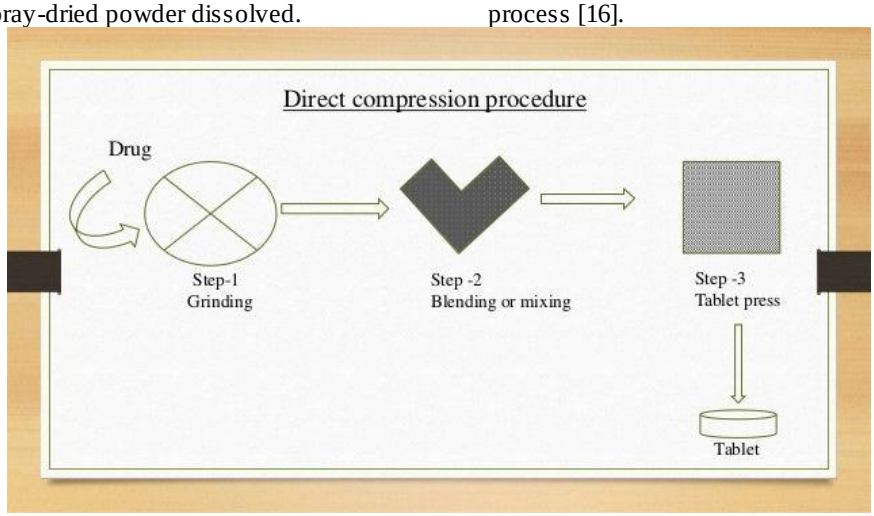

Figure 2: Direct Compression Process

CHALLENGES OF FORMULATING RAPID DISINTEGRATING TABLETS[15]

1. Palatability

1.Palatability When considering most medications are indigestible, Drug delivery systems that quickly disintegrate frequently include the pharmaceutical in a taste-masked form. The active chemicals in delivery systems are released when the patient's mouth, dissolve or disintegrate.

2. Mechanical Strength

Fast-dissolving tablets that disintegrate in the oral cavity must primarily be made of a soft molded, highly porous the matrix or compacted into tablets with a small compression force. This makes the tablets brittle, friable, and challenging to handle, and it is often necessary to use specialized peel-off blister packaging, that may increase the cost.

3. Hygroscopicity

A number of oral disintegrating dosage forms are hygroscopic, meaning that normal temperature and humidity ranges cause them to lose their physical integrity. As a result, they need to be kept dry, which calls for particular product packaging.

4. Amount of Drug

ODTS technology are limited by the amount of medications that can be contained in each unit dose. For medications that dissolve poorly, the dosage in lyophilized form must be under 60 mg, and less than 400 mg for drugs that are insoluble. This characteristic presents a special challenge when creating oral films and wafers that dissolve quickly.

5. Aqueous Solubility

Water-soluble medications provide a number of formulation challenges because they produce eutectic mixtures, which lower the freezing point as well as produce glassy solids that may collapse when dried because the sublimation process loses supporting structure.

6. Size of Tablet

The size of the tablet determines It's easy to take. It has been reported that tablets that are 7-8 mm in size are easy to take, while tablets that are longer than 8 mm was the easiest to handle.

7. Mouth Feel

FDTs shouldn't break in the oral cavity. larger particles. The Particles that are produced during the breakdown of the FDTs must be as small as possible. In addition, the mouthfeel is improved by the inclusion of flavours the cooling agents, such as menthol. In addition, the mouthfeel is improved by the inclusion of flavours the cooling substances like menthol. Mouth feel-FDTs shouldn't fragment into larger particles in the oral canal. Additionally, adding flavours and cooling ingredients like menthol enhances the texture.

EVALUATION OF FAST DISINTEGRATING TABLETS (FDTs)

1. Appearance and Organoleptic Properties

The general appearance of the FDT provides preliminary information regarding its identity and acceptability. It includes factors such as color, shape, surface texture, and uniformity. A uniform appearance ensures batch-to-batch consistency and contributes to consumer confidence. Organoleptic evaluation includes the assessment of taste, odor, and mouthfeel, which are especially critical for FDTs as they dissolve in the oral cavity.

2. Tablet Thickness and Diameter

The thickness and diameter of FDTs must be consistent for uniform packaging and dosing. These parameters are measured using a digital Vernier caliper or micrometer screw gauge. Significant variations may indicate problems in granulation or compression processes, which could affect disintegration and dissolution behavior.

3. Weight Variation Test

This test ensures that each tablet contains the proper amount of drug substance. According to pharmacopeial guidelines (e.g., USP, IP), 20 tablets are individually weighed and compared to the average tablet weight. Tablets must fall within ±5% or ±10% of the average weight, depending on their mass. Any deviation can result in dosage inconsistency and therapeutic failure.

4. Hardness (Crushing Strength)

Although FDTs must disintegrate rapidly, they must also possess sufficient mechanical strength to withstand handling during manufacturing, packaging, and transport. Tablet hardness is measured using instruments like the Monsanto or Pfizer hardness tester. Ideally, FDTs should have a hardness in the range of 2–4 kg/cm² to balance between mechanical integrity and rapid disintegration.

5. Friability Test

Friability measures the resistance of tablets to abrasion and chipping. It is evaluated using a Roche friabilator, where tablets are subjected to rotational stress. Tablets are weighed before and after 100 revolutions, and the percentage weight loss is calculated. A friability below 1% is generally acceptable, indicating good mechanical strength and formulation stability.

6. Disintegration Time

This is the most critical evaluation parameter for FDTs. It measures the time taken by the tablet to break down into smaller particles in a suitable medium (usually water at 37±0.5°C) without using any disk in the disintegration apparatus. The United States Pharmacopeia (USP) stipulates that FDTs should disintegrate within 30 seconds to 3 minutes, depending on the product. Faster disintegration ensures quicker onset of action and improved patient compliance.

7. Wetting Time

Wetting time is an indirect measure of the hydration capacity and correlates with disintegration time. A circular piece of tissue paper is placed in a Petri dish with a water-soluble dye (like eosin), and the tablet is placed on it. The time taken for the dye to reach the upper surface of the tablet is recorded. A shorter wetting time indicates faster water penetration and better disintegration performance.

8. Water Absorption Ratio (R)

This test quantifies the tablet's ability to absorb water, which is critical for rapid disintegration. A pre-weighed tablet is placed on a saturated tissue paper in a Petri dish, allowed to absorb water, and weighed again. The water absorption ratio is calculated as:

R = 100 × (Wa - Wb) / Wb

where **Wa** is the weight after absorption and **Wb** is the weight before absorption. A higher water absorption ratio corresponds to a better disintegration profile.

9. Drug Content Uniformity

Each FDT must contain the active pharmaceutical ingredient (API) within the specified limits (usually 85% to 115% of the label claim). Ten tablets are randomly selected, crushed, and analyzed using suitable analytical techniques like UV spectroscopy or High-Performance Liquid Chromatography (HPLC). Uniformity ensures dose accuracy and therapeutic consistency, especially important in low-dose or potent drug formulations.

10. *In-Vitro* Dissolution Studies

Dissolution testing provides insight into the drug release behavior of FDTs. It is conducted using the USP Dissolution Apparatus II (Paddle method) at 50–100 rpm in media such as simulated saliva fluid or phosphate buffer (pH 6.8). Samples are withdrawn at predetermined intervals and analyzed spectrophotometrically. A faster dissolution rate often correlates with enhanced bioavailability and quicker onset of action.

11. Taste Evaluation

Since FDTs dissolve in the oral cavity, taste is an essential quality parameter. Poor taste can lead to non-compliance, especially in pediatric or elderly patients. Taste evaluation may be done using a volunteer sensory panel or in vitro tools like electronic tongues. Techniques like complexation, coating, or use of sweeteners are often employed to mask bitterness.

12. Moisture Uptake Studies

Due to their hygroscopic nature, FDTs are susceptible to moisture, which can alter their mechanical strength and disintegration time. Moisture uptake studies are carried out by exposing tablets to controlled humidity conditions and monitoring changes in weight and performance. Appropriate packaging (e.g., aluminum blisters) is recommended to preserve tablet stability.

13. Stability Studies

Stability testing under ICH-recommended conditions (e.g., 40°C ± 2°C and 75% RH ± 5%) helps determine the shelf life of FDTs. Periodic evaluation of key parameters such as hardness, friability, disintegration time, drug content, and dissolution profile ensure that the product maintains its quality over time. These studies guide storage conditions and expiration dating [17].

CONCLUSION

Fast disintegrating tablets are novel dosage forms created specifically to certain issues associated with conventional solid dosage forms, such as the difficulty that fast-disintegrating tablets represent an innovative dosage form created specifically to certain issues associated with conventional solid dosage forms, such as the difficulty that geriatric and pediatric patients have in swallowing tablets. Fast disintegrating tablets are formulated to break down or dissolve quickly in saliva, typically within a span of less than 60 seconds (5-60 seconds range). Fdt dosage forms cater to a diverse patient demographic, such as children, the elderly, and those who have trouble swallowing. These forms' capacity to offer the benefits of liquid medication is one of their main advantages. while being solid preparations. This allows patients to take in the prescribed amount of water at any time without discomfort. These products and technologies fulfil a distinct medical necessity and present clinical benefits.

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