

Fast Dissolving Tablets: A Comprehensive Review of Formulation Strategies and Technological Advancements

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ABSTRACT

Fast-dissolving tablets (FDTs), (ODTs) or (MDTs) are one of the most sophisticated types in oral solid dosage form. This study includes developments in formulation, excipient use, manufacturing technologies, QC approaches, and therapeutic uses. FDTs disintegrate in the mouth within 60 seconds without needing water. It is significantly beneficial for patients with dysphagia, pediatric, geriatric and psychiatric individuals. The market for orally disintegrating tablets was expected to increase from USD 14.3 billion to USD 29.0 billion by 2033. It reflects an expected compound annual growth rate of 8.2%. This study exhaustively analyses various production methods as direct compression, lyophilisation, spray drying, sublimation and three-dimensional (3D) printing. A new excipient system involving synthetic super-disintegrants and natural gums is able to mask taste using microencapsulation, ion-exchange resins, and cyclodextrin complexation. The essential incorporation of the Quality by Design (QbD) approach, which cover Design of Experiments (DoE), response surface methodology, and the Quality Target Product Profile (QTPP) framework. Particular emphasis is given to nanotechnology-based FDTs, comprising formulations loaded with nanoparticles and lipid carriers with nanostructures, which have significantly improved the bioavailability of BCS Class II and IV medications. This review offers pharmaceutical scientists, formulation specialists, and regulatory experts a definitive, evidence-based resource on the current advancements in fast-dissolving tablet technology.

Keywords: Fast dissolving tablets, orally disintegrating tablets, superdisintegrants, taste masking, lyophilization, 3D printing, QbD, nanotechnology, bioavailability, patient compliance, direct compression, dysphagia

INTRODUCTION

Historically, the oral route has been the predominant route of administration in the pharmaceutical industry, with over 85% of marketed drugs administered orally [36]. Tablets and capsules are still the gold standard of oral dosage forms because of their manufacturability, dosing accuracy, stability and patient familiarity [97, 134]. However, a clinically important and frequent problem is the difficulty swallowing solid dosage forms experienced by many patients (26–55% adults, 50–70% in pediatric populations and 35–60% in elderly patients) [49, 59].

Dysphagia, or difficulty in swallowing, is related to head and neck cancer, esophageal disorders,

neurological conditions and age-related physiological changes. It is also associated with decreased saliva production and decreased swallowing reflex. According to Mayo Clinic Proceedings, about 10–33% of older people suffer from dysphagia. This population also suffers from multiple chronic illnesses requiring polypharmacy [60]. Medication non-adherence is aggravated not only by physical difficulties but also by psychological resistance to taking tablets, especially in mental patients.

Fast dissolving tablets (FDTs) are also known as mouth dissolving tablets (MDTs), oral disintegrating tablets (ODTs) or rapid-melt tablets in the regulatory arena. FDTs are a revolutionary technology in the science of oral dosage formulations. In the Ph. Eur.

and USP they are defined as solid oral dosage forms that dissolve or disintegrate in the oral cavity within 60 seconds when placed on the tongue, without the need for water [2, 62]. Since the 1980s, Zydis technology and its first commercial Claritin Reditab were introduced by Cardinal Health. The MDTs has grown exponentially both in terms of academic research output and commercial product availability [33, 38].

Valued at USD 14.3 billion in 2024, the market is forecast to grow to USD 29.0 billion by 2033 at a CAGR of 8.2% [37, 45]. The Business Research Insights estimates a parallel market of ODT excipients of USD 17.87 billion in 2023 expected to increase to USD 24.19 billion by 2032 [9]. These numbers highlight the business needs and society demand that are stimulating FDT technology innovation. In the last decade, significant progress has been made in many aspects of FDT research; discovery and optimization of next generation superdisintegrants from natural polymers; incorporation of nanotechnology platform for overcoming solubility and bioavailability issues; infusion of systematic design rigor through Quality by Design (QbD) methodologies for FDT formulation development; and the extension of regulatory guidance frameworks by the USFDA and EMA to accommodate such innovations as 3D printing for personalized manufacturing of FDTs. The aims of this study are: (i) to define the advantages, limitations and regulatory definitions of FDTs; (ii) to review formulation excipients and mechanisms of action; (iii) to critically discuss the manufacturing technologies and highlight the innovations in the last decade; (iv) to discuss taste masking strategies; (v) to highlight the evaluation methodologies and quality standards; (vi) to review the integration of the QbD framework; (vii) to discuss about nanotechnology application in FDTs; (viii) to survey marketed product and therapeutic applications; and (ix) to outline future perspectives and unresolved challenges.

2. Background, Definitions and Regulation

2.1 Definition and Nomenclature

Different regulatory jurisdictions have different terms for FDTs, and this will lead to variability of the literature. An ODT is defined by U.S. FDA as a “dose dosage form that is rapidly disintegrated in the mouth, typically in seconds, after placement on the tongue” [17]. The European Pharmacopoeia uses the term orodispersible tablets (ODTs) and sets a maximum of

three minutes for the tablets to disintegrate on testing in accordance with the Ph. Eur. The 2.9.1 disintegration test is from [16]. Per USP<701> (USP-NF, 2024), limits the amount of time it takes for a disintegration in water at $37^{\circ}\text{C} \pm 2^{\circ}\text{C}$ to be no more than 30 s. The different synonyms used in literature include mouth-dissolving tablets, rapid-dissolving tablets, fast-disintegrating tablets, melt-in-mouth tablets, quick-dissolving tablets, rapid-melt tablets, porous tablets and rapimelts [39, 47, 56, 74, 78, 84, 108, 115]. The terms "FDTs" and "ODTs" are used synonymously for this review, in line with the prevailing terminology in recent literature.

2.2 Historical Evolution

FDTs were first conceptualized in the 1970s when researchers began to understand that the ability to take oral dosage forms is a big compliance challenge. The Zydis system is the first patented FDT technology, which was developed by Cardinal Health (formerly R.P. Scherer), and commercially released in 1986 with the active ingredient loratadine (Claritin Reditab). The freeze drying based platform resulted in a porous and fragile tablet which dissolved in oral cavity within seconds. During the next few decades, other technologies were designed: the WOWTAB technology (Yamanouchi Pharma Technologies), the OraSolv and DuraSolv systems (CIMA Labs), the FlashTab (Ethypharm) and the Flashdose technology (Fuisz Technologies, later named Biovail) [34, 83]. Generic ODT market entry increased product diversity significantly in 2010-2020, as the patent expiries of certain reference listed drugs stimulated other market entrants. It has been a decade of development of these early technologies and emergence of entirely new manufacturing concepts such as 3D printing, providing significant new dose customization and dosage form architecture options [22, 51, 72, 82].

2.3 Regulatory Considerations

Specific guidance has been issued by the regulatory agencies concerning development of FDTs. The USFDA has released “Guidance for Industry: Orally Disintegrating Tablets” (2008) which offers guidance on dissolution and disintegration testing, taste testing, bioequivalence testing, and labelling. The guidance categorizes the disintegrating tablets into two types: rapidly dissolving tablets (dissolution of 85 % of the drug substance in 15 minutes in 900 mL of the various media, USP apparatus II) and disintegrating tablets (only the property of disintegrating is required,

but the dissolution of the drug substance does not necessarily have to be rapid). [17, 18].

The European Medicines Agency (EMA) Note for Guidance on Pharmaceutical Development (ICH Q8) and the ICH Q9 (Quality Risk Management) and ICH Q10 (Pharmaceutical Quality System) guidelines combine to provide a framework for QbD, which ODTs should be developed and validated within. The guidelines have been incorporated into the expectations of both EMA and FDA for a novel oral solid dosage form and require demonstration of a robust design space critical quality attributes (CQAs) and critical process parameters (CPPs) [15, 24, 25, 26].

The WHO has also commented on ODT quality standards in its quality assurance model for procurement agencies, highlighting the special role of the ODTs for global applications in health, such as for assisting in the management of TB, malaria and the treatment of HIV in children [65]. This regulatory environment is dynamic as both FDA and EMA are continually refining their guidance in line with 3D-printed drugs and AI-driven formulation development processes.

3.0 Advantages, Limitations and Ideal Candidate Characteristics

3.1 Advantages of FDTs

FDTs offer several clinical and commercial benefits compared to traditional solid oral dosage forms, which are well documented in the recent literature [2, 35, 48, 58, 107, 116].

The waterless administration: FDTs can be given anywhere, anytime, without the need for water or other liquid, improving convenience for the patient in ambulatory, travel or emergency situations.

Convenience: Due to the absence of the swallowing burden, FDTs can enhance medication adherence, especially in children (2–12 years), elderly (aged >65 years) and psychiatric patients [32, 40].

Onset of action: Drugs are absorbed through buccal and sublingual mucosa, which allows them to enter the blood stream partially avoiding the first pass metabolism in liver, thus enhancing bioavailability and rapid onset of action [36].

FDTs may offer an alternative buccal/sublingual absorption route that bypasses first-pass metabolism

and gastrointestinal degradation that is pH dependent, which is particularly relevant for certain drugs that have high first-pass metabolism or pH-dependent gastrointestinal degradation [63, 127].

The advantage of stability over liquid formulations:

FDTs retain the stability issues of solid dosage forms, such as decreased risk of hydrolysis, oxidation, and microbial contamination. No large solid fragments after dissolution = reduced risk of aspiration, especially beneficial for patients following stroke with swallowing impairments. Regulatory agencies recognise the value of using FDTs as dosage forms for children and within the framework of the FDA Pediatric Research Equity Act (PREA) (EC 1901/2006, Paediatric Regulation [40]) FDTs are encouraged for children.

3.2 Limitations and Challenges

Although FDTs have many benefits, they are also known to have a number of inherent formulation and manufacturing challenges, and have been the focus of sustained research efforts in the past decade [49, 47].

- **Mechanical fragility:** FDTs, especially lyophilized, are very soft (hardness 1-2 N) and may be broken when handled, packaged or shipped. This requires special blister packing and handling procedures [92].
- **Poor formulations for rapid disintegrations and patient acceptance:** Drug doses higher than 400-500 mg make them not well suited for FDT formulations because the tablet mass required to achieve the desired dose increases, which will make the tablet more difficult to disintegrate rapidly and more unpleasant to swallow.
- **Taste Masking Complexity:** There is a significant number of APIs that are bitter or have an unpleasant taste, which must be taste masked before formulation into FDTs. This makes formulation more complicated and expensive.
- **Hygroscopicity:** FDTs are prone to absorbing water from the atmosphere that causes them to soften, lose porosity and decrease disintegration ability. Special packaging and storage conditions (usually 25°C / 60% RH) are required.
- **Capital and operation cost:** Some FDT manufacturing processes, such as lyophilization and 3D printing, have greater capital and operating expenses than direct compression.
- **Drug stability in the oral cavity:** Drugs that are susceptible to degradation by salivary enzymes or pH instability in the saliva may be degraded before they are absorbed.

3.3 Ideal candidate drug characteristics: ideal characteristics of drugs are described.

- Not all drugs are suitable for FDT formulation. The following are desired characteristics in an ideal drug product profile for FDT formulation [34, 35]:
- The molecular weight is less than 500 Da to allow permeation of mucosa.
- Does not exceed 400 mg (practical sized tablet)
- Short or no first-pass metabolism (or drugs that are designed to take advantage of pre-gastric absorption)
- The solubility is sufficient in the saliva or there is effective enhancement of solubility in the saliva.
- Rangonius flavor that can be masking treated to good effect.
- Remains stable at body temperature (37°C) and in the pH of saliva (6.2–7.4)
- Treatment of disease for which rapid onset is clinically significant (e.g. migraine, nausea, pain, anxiety)

4.0 Excipient Systems in Fast Dissolving Tablets

4.1 Superdisintegrants: The foundation of FDT technology Superdisintegrants are the most important class of functional excipients in FDT formulations. The superdisintegrants differ from the conventional disintegrants in their ability to disintegrate at low concentration (1-10% w/w), the disintegration occurring through three main mechanisms: (i) swelling, water absorbed causes an expansion force which breaks the tablet matrix; (ii) wicking (capillary action), water absorbed through the tablet, breaks the intergranular bonds; (iii) deformation recovery, the plastic deformation of the disintegrant particles during compaction is recovered on wetting, creating an internal stress [5, 12, 54, 101].

4.1.1 Synthetic Superdisintegrants During the review period, the three main superdisintegrants - crospovidone (crosslinked polyvinylpyrrolidone), croscarmellose sodium (crosslinked sodium carboxymethylcellulose) and sodium starch glycolate (crosslinked sodium carboxymethylstarch) - continued to be used as the workhorses in FDT formulation, with much literature on their optimization for new formulations [13, 57, 91]. Crospovidone (CP), commercially available as crosslinked polyvinylpyrrolidone under the trade name Kollidon CL (BASF), Polyplasdon XL (ISP) and Polyplasdon XL-10, acts as disintegrator mainly through the mechanisms of wicking and recovery from deformation. It has a very high water uptake (>100 mL/g) and the absence of ionogenic groups makes it suitable for a broad pH range. CP can

consistently be found to have disintegration times of 15 to 45 seconds at 2 to 5% w/w concentration in FDTs. Zhu et al. [69] showed 1.8-fold increase in relative bioavailability for the CP containing piperine FDTs over conventional tablets, which can be attributed to rapid disintegration and improved mucosal permeation.

Croscarmellose sodium (CCS, Ac-Di-Sol, FMC BioPolymer) works mainly by swelling and will swell by 4- to 8-fold when it comes in contact with water. The use of CCS in direct compression FDT formulations is especially effective at 5% w/w. However, its ionic nature makes it vulnerable to the interaction with cationic drugs, so it is important to analyze the drugs' compatibility. The enhanced combination of CP (3% w/w) and CCS (5% w/w) was used in the formulation of FDTs for prochlorperazine and a $t_{50\%}$ of 7.0 min was obtained which is comparable to the conventional tablet with a $t_{50\%}$ of 17.4 min [57].

The main action of sodium starch glycolate (SSG, Explotab, and Primojel) is by swelling with a water absorption ability of 600-800% of its own weight. With other superdisintegrants, SSG will be more effective in FDTs prepared by wet granulation, where other superdisintegrants could dissolve during the granulation process. In patient groups with sodium restrictions, however, this may be a drawback to the high sodium content of SSG.

4.1.2 Natural polymers

In recent years, however, natural-based superdisintegrants have garnered significant attention in the research field due to their better environmental and toxicological attributes and increased cost as compared to synthetic superdisintegrants [52, 66]. The naturally derived N-deacetylated chitin polymer chitosan was found to be an effective natural superdisintegrant in meloxicam ODTs with a disintegration time of 21 ± 3 seconds at a concentration of 4% w/w, which is similar to the CCS-containing formulations [13, 131]. This process is due to the combination of swelling in the acidic oral environment (The pKa of chitosan is about 6.5), and capillary driven wicking caused by the porous microstructure of chitosan.

Other natural superdisintegrants investigated during the reviewed period are isabgol husk which has achieved disintegration time of 20–30 seconds at 5%

in w/w by dual wicking and swelling action, banana starch modified with sodium chloroacetate which has achieved disintegration time of 27 ± 2 seconds in paracetamol FDTs [114], fenugreek seed mucilage (*Trigonella foenum-graecum*) tested in ondansetron FDTs and the disintegration time is 27 ± 2 seconds [53], *Lepidium sativum* mucilage which has been extensively investigated in aceclofenac FDTs using 3^2 factorial design with disintegration time of 27 ± 2 seconds [30] and gellan gum and xanthan gum which are noted as non-toxic, biodegradable and cost effective [66, 141, 147].

4.2 Fillers and Diluents

Most of the FDT formulations are composed primarily of fillers and diluents, which are very important in deciding the disintegration rate, hardness of tablet and patient acceptability. In FDTs, water soluble fillers were preferred because they are easily dissolved in saliva to leave no residue and provide a pleasant mouthfeel. The most commonly used FDT diluent is Mannitol (D-mannitol) which offers several important properties such as negative heat of solution, which provides a cool and refreshing sensation in the mouth, high water solubility (182 g/L at 25°C), low hygroscopicity, excellent chemical compatibility, and a distinct lack of cariogenicity [35, 105]. A large number of commercially available grades have been judiciously characterized in the FDT literature, such as Pearlitol SD100, Pearlitol 100C and granulated mannitol (Pearlitol 400DC). Other excipients include sorbitol, lactose (if lactase deficiency is not a problem), xylitol and microcrystalline cellulose (MCC, Avicel PH-102) which gives additional disintegration support due to its water-uptake capacity but not as good a mouth feel as mannitol [99].

4.3 Binders

The problem with the selection of binders for FDTs is that there is a balance required between the strength imparting properties and the hindering disintegration properties. The commonly used dry binders are polyvinylpyrrolidone (PVP K30 or K90) at 2-5% w/w and hydroxypropyl methylcellulose (HPMC) grades (E3 or E5) at 1-3% w/w. In some formulations, polyethylene glycols, PEG 4000 and PEG 6000, are used as a binder and a solubiliser. Low viscosity grades of HPMC and hydroxypropyl cellulose (HPC, Klucel LF) are preferred because they tend to have less effect on disintegration time. In FDTs, lubricants (mainly magnesium stearate, 0.25–0.5% w/w) should be used in the minimum amount because excessive

amount of hydrophobic lubricant covering the particles can significantly hinder water ingress and prolong its disintegration [30, 35, 113]

4.4 Taste Masking Agents

Taste masking is probably the most difficult step to accomplish in the formulation of many APIs. The oral cavity is equipped with around 10,000 taste buds which are sensitive to the bitter compounds at a concentration as low as 8 μ M. In the last decade, approaches to taste masking in FDTs have progressed a long way, and are discussed in detail in Section 7.

4.5: Sweeteners and Flavoring Agents

Sweeteners are an essential component of FDT palatability, helping to reduce the bitterness from the FDT and to improve its acceptability. Aspartame (180 $\times$ sweeter as sucrose), acesulfame potassium (200 $\times$ sweeter as sucrose), sucralose (600 $\times$ sweeter as sucrose) and saccharin are widely used at 0.1–1.0% (w/w) level. Mannitol and sorbitol are also sweet, giving some sweetness to the formulation. In the regulatory environment, there is growing interest in the use of natural sweeteners, such as those with “clean label” as alternatives to sucrose, including stevia (rebaudioside A, 200-300 times sweeter) and thaumatin (2000-100,000 times sweeter). Spray-dried microencapsulated flavors of mint, strawberry, orange, and tutti-futti have been used at 0.1–1.5% w/w as a flavor system to enhance sweetness and offer positive flavor cues [31]. The lecture covers the manufacturing technologies for fast dissolving tablets. The lecture is about the manufacturing technologies for fast dissolving tablets.

5. Manufacturing Technologies for Fast Dissolving Tablets

5.1 Direct Compression Direct compression (DC) is the most basic, economical and most commonly used process to manufacture FDTs at the industrial scale [10, 40, 46, 79]. It is a dry blending technique of the API with superdisintegrants, fillers, binders, lubricants and any other excipients that are needed for the tablet to function, followed by compression on a standard rotary tablet press. Advantage of DC over wet granulation and lyophilization is that it is free from thermal and solvent stress, thus suitable for moisture and heat sensitive APIs. In DC based FDTs, the formulation challenge is to achieve the simultaneous optimization of tablet porosity (which determines disintegration) and mechanical robustness of tablets during handling/packaging (which is determined by the tablet tensile strength). Extensive

investigations have been performed using DoE techniques for the optimization of the DC parameters of FDTs. Yamuna et al. [67] developed the superdisintegrant based on QbD approach systematically studying the effects of superdisintegrant concentration, compression force and mannitol to-MCC ratio on CQAs such as disintegration time, tensile strength, and drug dissolution rate. The use of directly compressible co-processed excipients like Ludiflash (BASF; mannitol/polyvinyl acetate/crospovidone), Pharmaburst 500 (SPI Pharma; mannitol/crospovidone/silicified MCC) or F-MELT Type C (Fuji Chemical; mannitol/microcrystalline cellulose/crospovidone) has significantly enabled the manufacturing of DC-FDTs, as they offer rapid disintegration, as well as good mechanical properties from one excipient system. The disintegration time of these coprocessed systems was found to be 15-30 seconds, with tablets having a hardness ≥ 3 kN [58, 98].

5.2 Lyophilization (Freeze-Drying)

The first commercial ODT products (Zydis technology) have been produced using lyophilisation, also known as freeze-drying, which are essential for thermolabile APIs, very fast disintegration (VFD) (≥ 3 seconds). The API and excipients, including a matrix-forming agent (gelatin, alginates or dextran), bulking agent (mannitol or sorbitol) and surfactant (typically polysorbate 80) are dissolved or suspended in an aqueous medium, which is then poured into the blister cavities and then frozen at temperatures ranging from -40°C to -70°C to convert the water to ice, and finally the ice is freeze-dried under vacuum, leaving a porous highly water-absorbing matrix [27, 42, 95, 132].

The lyophilized ODTs produced have disintegration time of 3-10 seconds and have very high dissolution rates, especially for water soluble APIs. The mechanical fragility of the freeze-dried ODTs (1–2 N) however requires special packaging (aluminum blister packs) and cannot be dispensed from multidose containers. Other manufacturing constraints are the high capital cost and slow throughput of lyophilization equipment. Some of these limitations were overcome with recent innovations: use of trehalose, sucrose or mannitol as cryoprotectant to prevent aggregation of nanoparticles during freeze drying, which enabled the incorporation of nanoparticulate APIs [3, 6, 68]; controlled nucleation

technologies improved freeze drying efficiency and the continuous lyophilization systems were explored to overcome the throughput limitations.

Recently, Party et al. [42] developed a nanosized piroxicam orodispersible lyophilizate by using the method of nanoprecipitation in combination with solvent diffusion and freeze drying. The lyophilizate containing the nanoparticles released the drug in 5 seconds and the bioavailability of piroxicam was enhanced due to the small size of the nanoparticles (220 ± 15 nm) and the rapid mucosal exposure.

5.3 Spray Drying

Spray drying has been used in two different ways for the manufacturing of FDTs: (i) for spray drying of co-processed excipients with optimized particle size, shape and surface area for production of DC-FDTs; and (ii) for microencapsulation of taste-masking coating materials before compression. The former application results in spherical porous particles having a very high surface area and excellent flow properties. Commercial spray-dried excipients available for FDT are the optimized particle morphology for direct compression ODTs, Parateck ODT (Merck KGaA) which is a spray-dried blend of mannitol and sorbitol [49, 58, 100].

5.4 Sublimation Technology

The sublimation technology, also known as the sublimation method or the solid-volatile inclusion method, is the technique using a solid that will sublime when heated during the compression of the tablet. The tablet is then compressed under normal compression and heated at high temperatures in a vacuum, causing the volatilizable solid to sublime, leaving very porous channels in the matrix. This creates a very high porosity making the surface area for water contact very large and the material readily disintegrates. In modern literature of FDT, camphor (with melting point of 175°C and sublimation point of 200°C) and menthol (melting point 43°C and sublimation point 200°C) are most commonly used subliming agents. The main restriction is the requirement of post-compression heating which could affect the thermolabile APIs [73].

5.5 Melt Granulation

The method of melt granulation (hot melt granulation) uses a meltable binder such as PEG 4000, PEG 6000, glyceryl monostearate, Compritol 888 ATO or Precirol ATO at amounts of 5–20% w/w and applies

it at elevated temperatures (50–80°C) without the use of solvents. The resulting granules have superior flow, are less dusty and when used in combination with super disintegrants have acceptable disintegration. Vemula et al. [63] used a melt dispersion approach combined with surface adsorption to prepare flurbiprofen FDTs which released 99.34% of the drug within 15 minutes and exhibited enhanced C_{max} in rats as compared to conventional tablets.

5.6 Wet Granulation

Wet Granulation is not a standard process in the manufacturing of FDTs because it increases the processing time and is vulnerable to dissolving water soluble superdisintegrants but it is applicable when the APIs have poor flow properties [122], the drug is prone to dusting or requested to include some specific particle size distribution. Wet granulation and drying followed by extragranular incorporation of superdisintegrant is a validated technique to ensure the integrity of function of superdisintegrants. Scaled-up processing of Fluidized Bed Technology (FDT) has been carried out using high shear wet granulation and fluidized bed drying, with good results [41].

5.7 Three-Dimensional Printing

Three-dimensional (3D) printing has become a groundbreaking manufacturing technology, especially for pharmaceutical dosage forms, and shows great potential for an application in FDT [22]; (3D printing ODTs, 2022). The major benefit of 3D printing is the capability to create highly customized dosage forms that are optimized for the weight, the PK profile and the ability to swallow of each patient, without the need of having any capital investment on traditional batch manufacturing machinery. Various 3D printing technologies have been tried to produce FDT. Fused deposition modeling (FDM) is a technique where a thermoplastic polymer filament is melted and extruded onto a platform layer-by-layer; thermoplastic polymer matrices such as hydroxypropyl methylcellulose acetate succinate (HPMCAS), polyvinyl alcohol (PVA) and Eudragit have been used to prepare FDM FDTs [23]. Direct powder extrusion (DPE) which does not require prefabricated filaments and directly extrudes powdered blends has been used with greater flexibility in the production of orodispersible film and tablet [43, 44, 80, 125]. Pediatric ODTs have been produced using semi-solid extrusion (SSE) and the final products are gummy like and have improved

acceptability [20, 50, 51]. The Binder Jetting 3D printing selectively jets liquid binder onto powder layers to construct FDTs, which have very fast disintegration rates, similar to those of lyophilized ODTs.

Apreece Pharmaceuticals got its first FDA approval for a 3D-printed pharmaceutical product in 2015, with the launch of levetiracetam (Spritam), a 3D-printed ODT using the ZipDose technology which is based on a binder-jet process. Once Spritam is swallowed by a sip of liquid, it disintegrates in 1-2 seconds making it possible to deliver high doses (250-1000 mg), which were not previously possible with conventional ODT manufacturing platforms. This historic authorization paved the way for 3D-printed pharmaceuticals in a regulatory avenue that has led to significant investments in 3D printing in the pharmaceutical sector [22].

On the research front, 3D printing has been used to prepare more complex FDT designs, such as multiple-layer tablets containing sustained-release and immediate-release components, as well as internal architectural complexity to control the disintegration rate of tablets, and even to tailor dosing for pediatric patients based on weight-based dosing algorithms [7, 21, 70, 88]. In 2023, the FDA published regulatory guidance specific to 3D printed drug products [19], which have direct relevance to the use of 3D printing in FDT.

6. Taste Masking Strategies

6.1 Challenges in Taste Masking for FDTs. The API will come into direct contact with taste receptors on the tongue and oral mucosa during the very short residence time before swallowed, making FDTs suitable for the evaluation of taste perception. This is a key formulation challenge for APIs that are bitter, or have an unpleasant taste, and for most antibiotics, antihistamines, antiepileptics and analgesics [87, 129]. When the taste is not masked effectively, the patient compliance benefit is a key component of the value proposition for the FDT is lost [31, 64].

6.2 Organoleptic Modification:

Sweeteners and Flavors The simplest ways of masking the taste are to add sweetening agents and flavorants to the formulation to mask the bitter taste elements or to out compete them. This method is suitable for mildly bitter APIs, but will not work well for highly bitter APIs. Common sweeteners used are

aspartame, acesulfame-K, sucralose, thaumatin and rebaudioside-A derived from stevia, which are selected by taste panel testing, and these are often mixed with cooling agents (like menthol) to mask the bitter flavor [49].

6.3 Microencapsulation

The coating of the drug particles with a thin polymer film forms a physical barrier between the API and the taste receptors and is known as microencapsulation. The microencapsulated FDT will disintegrate in the mouth, releasing the drug as coated microparticles that will only break down after being swallowed in the stomachs acidic pH 1-2 or in the intestine (pH 6-7.5) [138, 149]. The polymers used for taste-masking microencapsulation are Eudragit E100 (cationic polymer soluble at a pH<5), Eudragit EPO, cellulose acetate, ethylcellulose and shellac. Spray coating is the typical industrial microencapsulation process, which is carried out in a fluidized bed coater. The range of drug particle size targeted is 150-400 μ m to achieve the balance between taste masking efficiency (complete drug coating) and acceptable oral sensation (mouthfeel) [47, 76, 146]. The principle of flavor microencapsulation in chewing gums for taste masking was investigated thoroughly by Kaushik et al [31] and the results of this article were directly applicable to the FDTs as complex coacervation and spray drying techniques yielded 70–95% efficiency of encapsulation for flavor compounds.

6.4 Ion-Exchange Resin Complexation

Ion-exchange resins (IERs) were found to form drug-resin complexes (drug-resinates) in an ionic interaction mechanism which allows the release of the drug only in the presence of higher ionic strength gastrointestinal fluids (where the higher ionic strength of the gastrointestinal fluids causes the competition between the drug and other electrolytes to be released from the resin). The most commonly used IERs used for taste masking in FDTs are Amberlite IRP-69, a sulfonated polystyrene cation exchange resin and Amberlite IRP-88, an acrylic acid polymer anion exchange resin. Resinate formation decreases the solubility of the drug in saliva, while allowing the drug to be released in the GI tract. The technology has proven to be very efficient for cationic basic drugs (antihistamines, decongestants, antitussives) which have high affinity for sulfonate resin groups. The drug-resin complexes thus obtained can then be further coated with the water-insoluble polymers to further delay the oral release [64].

6.5 Cyclodextrin Inclusion Complexes

The most common are cyclic oligosaccharides, cyclodextrins (CDs) which consist of glucose units arranged in the form of a truncated cone, with a hydrophobic cavity and a hydrophilic exterior, and are especially useful for sequestering the API inside the CD cavity making it less available to the oral taste receptors, the most commonly used being β -cyclodextrin (7 glucose units, cavity diameter 0.6–0.65 nm) followed by hydroxypropyl- β -cyclodextrin (HP β CD) which has excellent aqueous solubility. The taste masking, improved aqueous solubility (for BCS class II drugs) and improved chemical stability [30, 53] are achieved in a single step with the complexation of the drug in the CD.

In a recent study, midazolam/ γ -cyclodextrin ODFs were developed using the DPE 3D printing method, which has shown that the inclusion complex formed in-situ during the DPE 3D printing process combines taste masking, improved bioavailability due to sublingual absorption, and manufacturing efficiency in a single process.

6.6 Adsorption on Carriers

Taste masking by the adsorption technique consists of binding the drug to an insoluble adsorbent like magnesium aluminometasilicate (Neusilin US2), silicon dioxide or kaolin which bind the drug molecules to their surface and lower drug solubility in saliva. The drug that is adsorbed will be removed in the acidic gastric pH or by the competitive displacement effect of more strongly adsorbing species. This method has been implemented in combination with surface-adsorption techniques in melt-dispersion granulation to enhance solubility, while also masking the taste of the drug at the same time [63].

7. Methodology for the evaluation of FDTs and quality standards

7.1 Disintegration Testing

Disintegration testing is the most basic quality parameter of FDTs. Various methods have been reported in the literature and pharmacopoeias. The USP<701> disintegration test is performed in a basket-rack assembly with 900 mL of distilled water at $37 \pm 2^\circ\text{C}$ while for FDTs, the test is modified to be conducted in a petri dish with only 2 mL of water reflecting the small amount of saliva available in the mouth at rest (2–3 mL). The Ph. Eur. According to

2.9.1 method, ODTs should break down in water at room temperature of 15-25°C in three minutes. According to the Japanese Pharmacopoeia (JP XVIII), it should disintegrate within 30 seconds of 5 mL of water at 37°C. In vitro approaches which try to simulate in vivo oral disintegration conditions are the ERT (electronic tongue-related test) using modified Viva apparatus (Erweka) with 2 mL of the dissolution medium at 37°C, and the Texture Analyzer Method, in which the force and the displacement profile are measured during compression of a wetted tablet by a probe. The ultimate standard for disintegration testing is done in vivo using human patients; typically, a panel of 6-12 volunteers with a common human condition are used to record the time from placement on the tongue to complete disintegration [29, 62, 102, 118].

7.2 Dissolution Testing For FDTs,

Dissolution is performed in either USP apparatus II (paddle apparatus) or USP apparatus I (basket apparatus) usually in 900 mL of either phosphate buffer pH 6.8 or simulated gastric fluid (SGF, pH 1.2) at 37°C and 50-75 rpm. Two-phase dissolution model (organic solvent layer on top of aqueous buffer) has been suggested for FDTs that would require predominant buccal or sublingual absorption. The discriminatory dissolution conditions for the dissolution method need to be verified to confirm if the dissolution method has the ability to differentiate between formulations having different dissolution rate and/or bioavailability profile [18, 67].

7.3 Mechanical Strength Parameters

Hardness of tablets (crushing strength) is determined by a hardness tester (e.g. Monsanto, Erweka, Schleuniger). Hardness values for FDTs range from 3–8 kN and higher hardness will mean slower disintegration time.

The Roche friabilator values (USP<1216> at 25 rpm for 100 revolutions) must be $\leq 1\%$ for conventional tablets and at least the same for FDTs, but less important for individually blistered products due to special handling.

The hydrophilic character of FDT matrix can be further characterized by wetting time and water absorption ratio determined by measuring the time required for complete wetting of the tablet on the tissue paper soaked with 0.5 mL of water, visually. In academic publications, tensile strength ($TS = 2F/\pi Dt$,

where F is the breaking force, D is the diameter, and t is the thickness) is the most preferred mechanical parameter because it is a normalization that is based on the geometric shape of the tablet [35, 57, 92].

Content uniformity is tested in each USP<905> (Uniformity of Dosage Units) with acceptance criteria of 85–115% of the claimed amount on the label and the relative standard deviation (RSD) is within 15%.

The drug release kinetics from FDTs are analyzed by fitting drug dissolution data into zero-order, first-order, Higuchi, Korsmeyer-Peppas and Hixson-Crowell models to explain the drug release mechanisms [49, 63].

Organoleptic and Palatability Assessment:

The evaluation by human taste panel is based on numerical scores assigned by trained volunteers on 5-point scale for the following attributes: bitterness, sweetness, grittiness and overall acceptability. Objective electronic tongue (e-tongue) systems with cross-reactive sensor arrays, such as potentiometric, voltammetric or impedimetric sensors, are now gaining in use, and already there are correlation with the clinical palatability data [64].

Stability Testing

FDTs should be tested for stability according to the ICH Q1A(R2) guidelines: long-term (60%RH, 25°C, 12 months), intermediate (65%RH, 30°C, 6 months) and accelerated (75%RH, 40°C, 6 months). Specific stability protocols for HDT tablets involve testing at 75%RH since humidity is particularly important when it comes to the hardness, disintegration time and integrity of taste masking. Generally, the push-through aluminum-aluminum blister (cold-form foil) packaging system needs to exhibit good moisture barrier properties. The photostability studies are carried out for light sensitive APIs according to ICH Q1B [47, 62, 148].

8.0 Fast Dissolving Tablet Development: Quality by Design (QbD)

8.1 QbD Framework for FDTs

ICH Q8, ICH Q11 and ICH Q12 guidelines are the formalization of the Quality by Design (QbD) paradigm in pharmaceutical development, which is a paradigm shift from the traditional empirical trial and error optimization to design [24, 71, 86, 143]. The QbD framework for FDTs starts with the definition of the Quality Target Product Profile (QTPP) which is a

potential profile of the desired quality attributes for an FDT that would be required to provide the desired patient benefit and regulatory approval. Some key QTPP parameters for an FDT are: disintegration time (≤ 30 seconds), drug content (95–105% of label claim), hardness (3–8 kN), friability ($\leq 1\%$), dissolution (NLT 85% within 15 minutes), moisture content ($\leq 2\%$) and taste acceptability score ($\geq 4/5$) [41, 67, 150]. From QTPP, Critical Quality Attributes (CQAs) those quality attributes which must be within certain limits to ensure the desired quality of the product are then identified. In the case of FDTs, there are usually a number of criteria, such as disintegration time, dissolution rate, tensile strength, drug content uniformity, palatability, etc.

8.2 The Critical Material Attributes (CMAs) and Critical Process Parameters (CPPs) are identified during the risk assessment process, such as Ishikawa (fishbone) diagram, Failure Mode and Effects Analysis (FMEA) and Risk Ranking and Filtering. The first method is to use Design of Experiments (DoE) to map, empirically, the relationship between CMAs/CPPs and CQAs, resulting in a Design Space where variations of manufacturing parameters do not affect the product quality. The DoE application in FDT optimization will be discussed. Different types of DoE designs have been used in optimization of FDTs in various literature. Initial screening of critical variables is done using full factorial designs (2^2 , 2^3 and 3^2).

8.3 Response surface methodology (RSM) is used to optimize the formulations using Box-Behnken design (BBD), central composite design (CCD) and D-optimal designs [130, 137]. The polynomial models established by Kaur et al. [30] with the concentrations of the β -cyclodextrin and *Lepidium sativum* mucilage used in the FDTs of aceclofenac and their corresponding factor levels (disintegration time and dissolution efficiency, respectively) illustrate this approach.

Vemula et al. [63] used Plackett-Burman Design to screen 11 variables in the FDTs of flurbiprofen, and then Box-Behnken Design to evaluate the three most significant screening variables (superdisintegrant concentration, melt-dispersion temperature and surface adsorption time). The best formulation had the highest bioavailability of 1.38-fold in rats compared to the conventional tablet, with the value of Q15 being $99.34 \pm 1.24\%$.

Yamuna et al. [67] used a 3^2 design to develop the FDT using QbD approach, where the Physicochemical properties (disintegration time and tensile strength) were selected as CQAs, and their results showed that the developed Design Space was able to predict the performance of the FDT.

Likewise, Triboandas et al. [61] optimized itraconazole amorphous solid dispersion tablets, employing a 3^2 factorial design to assess the effect of inorganic salt type and concentration of Avicel on the disintegration time and tensile strength, to obtain the Design Space of both round and oblong tablet geometries.

In this course, students will be able to learn how to build AI/ML models. Another frontier in the development of FDTs is the incorporation of algorithms such as AI and ML into frameworks of QbD. In order to minimize the experimental effort required for conducting DoE studies, artificial neural networks (ANNs), random forests, support vector machines (SVMs) and Gaussian process regression are used to predict the FDT CQAs from the formulation variables. These methods can be useful in high dimensional formulation spaces that are not suitable for conventional DoE designs.

In this review, 42 ML studies were published and the number of FDTs were about 15% of the total published ML studies [28, 153]. The combination of AI-driven formulation design and high throughput experimentation (HTE) platforms generating and testing miniaturized FDTs in a 96-well plate format is a promising avenue for greatly improving the FDT development time [41].

9. Fast Dissolving Tablets (FDT) with the help of nanotechnology.

9.1 At what time to integrate nanotechnology? The main formulation challenge of the FDTs is the very low aqueous solubility of BCS class II drugs, which are considered to be highly permeable and exhibit low aqueous solubility, and BCS class IV drugs, which are low permeable and low aqueous soluble with a total of 70-80% of new chemical entities (NCEs) in the pharmaceutical development pipeline [1, 93, 120]. Nanotechnology can be applied to reduce the particle size to nanometer size (1-1000nm) which gives very large surface area of the drug particles in contact with dissolution medium, thus increasing dissolution rate

which is proportional to the surface area (Noyes-Whitney equation); it is possible to alter the solid-state properties of the drug in order to gain an increase in the intrinsic dissolution rate; it is possible to reduce the thickness of the diffusion layer [106, 112, 151].

9.2 Nanoparticle-Loaded FDTs

The nanosuspensions, a stable colloidal dispersion of nanosized drug particles stabilized by surfactant and polymeric stabilizer, is the most widely studied nanotechnology platform that is suitable for integration in an FDT. Media milling (NanoCrystal technology, Elan), high-pressure homogenization (Microfluidics) and precipitation are used to prepare the drug nanoparticles [85, 140] which are then integrated in the FDT by granulation, spray drying or direct compression. The same authors [42] were able to completely disintegrate orodispersible lyophilizates in 5 s with the same piroxicam nanoparticles (220 ± 15 nm) method but with a significantly higher dissolution rate and bioavailability even in the presence of food. Sharifi et al. [55, 89] studied the use of electrospun nanofibrous mats of diclofenac sodium in combination with the use of superdisintegrant showed that the surface area of electrospun fibers ($10\text{--}10,000$ m²/g) significantly improved the drug release when compared with conventional formulations based on microspheres. The Khan et al. [32, 119, 133, 152, 154] systematic review on Nanostructure-based formulations for ODTs in paediatric use comprehensively discussed the methods of preparation of nanoparticles and their platforms such as polymer coated nanocapsules and nanostructured lipid carriers as platforms suitable for paediatric ODT development.

9.3 Amorphous Solid Dispersions

Amorphous solid dispersions (ASDs) render crystalline APIs in an amorphous state that is dispersed within a polymer matrix resulting in a dramatic increase (sometimes 10-100-fold) in the apparent solubility of BCS Class II drugs by keeping the drug in a supersaturated, high-energy amorphous state. During the review period, the hot-melt extrusion (HME) and spray drying processes with HPMC, PVP, PVPVA, HPMCAS or a combination of these were among the most common processes used to formulate ASD, while FDT formulation was used in second place [11, 104]. Triboandas et al. [61] have prepared Itraconazole-Kollidon VA64 ASDs using HME and optimized tablet formulations by inorganic salts (KCl)

which resulted in rapid disintegration (as per ODT requirement) along with significantly higher dissolution rate compared to the crystalline itraconazole. According to the IJPSDR study (2025), in the direct compression study (based on QbD) the optimum process achieved the 99.11% drug release in 30 minutes and validated by the statistical DoE analysis.

9.4 Nanostructured Lipid Carriers

The second generation of solid lipid nanoparticles (SLDN), nanostructured lipid carriers (NLCs), are composed of a blend of solid and liquid lipids, which are not perfectly ordered, and are able to accommodate a drug, and release it slowly, whilst preventing degradation. They have been successfully loaded into matrices based on FDT (adsorbed on porous carriers or granulated) with drugs with BCS Class II like carbamazepine, simvastatin and rivaroxaban. A QbD-driven development approach was employed by Bajwa et al. [8, 77] to develop NLC loaded FDTs of an antimalarial drug of BSC class II which showed 2.8-fold improvement in the oral bioavailability compared to the conventional tablet in preclinical studies (AAPS PharmSciTech, 2022).

10. Therapeutic applications and marketed products

10.1 The following are CNS and Psychiatric Indications: The central nervous system (CNS) therapeutics segment accounted for the biggest share of the ODT market and is expected to be the most lucrative segment on the market due to the high prevalence of neurological and psychiatric diseases and the specific compliance challenges in this patient population. Cognitive impairment, fraudulent attempts to avoid the effects of medication (cheekpouch) and dysphagia resulting from extrapyramidal effects from the use of antipsychotics are common reasons for non-adherence among patients with schizophrenia, bipolar disorder and major depression [22, 37, 128, 144, 145].

10.2 There are marketed ODT products available in this segment of aripiprazole ODT (Abilify Discmelt, Otsuka), clozapine ODT (FazaClo, Jazz Pharmaceuticals), a combination of aripiprazole and olanzapine (Saphronia, Allergan), olanzapine ODT (Zyprexa Zydis, Eli Lilly), mirtazapine ODT (Remeron SolTab, Organon), and lorazepam ODT (Ativan sublingual, Pfizer) as well as risperidone ODT (Risperdal M-Tab, Janssen) [121, 124]. The Zyprexa Zydis formulation, made by lyophilization,

breaks down in under 5 seconds and clinical studies have shown that this form has much better adherence rates than the regular tablet formulation of Zyprexa [34]. Levetiracetam ODT (Spritam, Aprelia) is the landmark 3D printed ODT, which disintegrates in 1-2 seconds and can be taken in high doses (250-1000 mg) [22]. Anti-emetic & Anti-gastrointestinal indications Ondansetron ODT (Zofran ODT, GlaxoSmithKline; various generics) is a good example of the ideal drug to be an FDT; it is a relatively low dose drug (4 mg, 8 mg) with a patient population that is often not able to take conventional tablets because of severe nausea (cancer patients undergoing chemotherapy, post-surgical patients). There is a lot of literature available for the optimization of the formulation of Ondansetron ODT. Shahtalebi et al. [53] showed that fenugreek seed mucilage can be used as a natural superdisintegrant to form tablet formulation of ondansetron with successful result. Other well established marketed products in this segment include metoclopramide ODT, domperidone ODT and pantoprazole ODT [4, 117]. The use of analgesics and anti-inflammatory is an application

10.3. FDTs have one of their applications, rapid pain relief, that has a direct correlation between the rate of dissolution and onset of action and patient benefit. Examples of prominent marketed products include Ibuprofen ODT (Advil Quick-Dissolve, Pfizer), aspirin ODT (Bayer Quick-Release), rizatriptan ODT (Maxalt-MLT, Merck) and sumatriptan nasal ODT. Rizatriptan ODT is especially useful in the treatment of migraine, because nausea and gastric stasis are common occurrences during migraine attacks and affect the conventional tablet absorption. In several pharmacokinetic studies completed, rizatriptan ODT has been shown to be rapidly dissolved in the buccal cavity, resulting in an accelerated absorption (Tmax is ~1 hour compared to ~1.5 hours in the conventional tablet formulation) [34, 58, 75]. In the research literature, the ODTs for poorly soluble NSAIDs such as piroxicam, meloxicam, aceclofenac and diclofenac have been extensively studied. The dramatic dissolution enhancement of piroxicam was obtained using nanosizing by Party et al. [42]. Draksienė et al. [13] showed that the chitosan could be used as a superdisintegrant for the development of an effective ODT formulation of meloxicam. To enhance the drug loading capacity of ODT based on diclofenac sodium, Sharifi et al. [55] used electrospun nanofibers.

10.4 Cardiovascular Applications

Examples of cardiovascular drugs that are formulated as FDTs include isosorbide dinitrate sublingual tablets (which are essentially ODTs for angina), nitroglycerin sublingual tablets, captopril ODT, metoprolol ODT and valsartan ODT [94, 109, 123, 139, 142]. Pre-gastric absorption of nitroglycerin and isosorbide dinitrate is an important pharmacokinetic benefit of the ODT formulations, by avoiding hepatic first-pass metabolism, which gives rapid anginal relief. One recent study, by Springer et al., cited above (doi:10.1007/s12247-025-09983-6) has been on the management of hypertension using FDTs, specifically, the study investigated the QbD optimized valsartan FDTs, which were able to release the drug completely in 20 minutes, with a disintegration time of 28±2 seconds. The use of rivaroxaban ODT for dysphagia [4, 135] has been investigated for patients with dysphagia. This unit is about children's and elderly formulations. The main target groups for the use of FDT technology are the pediatric and geriatric patients. The WHO EMLc is now increasingly including ODT formulations, especially in the field of HIV antiretroviral therapy (pediatric lopinavir/ritonavir mini-tablet in a small amount of water) anti-malarial therapy (artemether-lumefantrine ODT) and antibiotic treatment of common childhood infections. They conducted a systematic review of ODTs for Paediatric Use [40] which reviewed 90 publications up to 2024 on ODT development specifically for children and found direct compression is the predominant method used for manufacturing ODTs in the paediatric population and taste masking the most important formulation challenge.

Artemether-lumefantrine and amoxicillin trihydrate ODTs combination products have been tested in the field of clinical practice in common childhood diseases [14, 90]. FDTs are particularly beneficial to adherence in geriatric patients' polypharmacy regimens. Data suggest that individuals older than 65 years (13–17% of the world's population) use about 35–40% of all prescribed drugs and that a large proportion of them (one-third to half) experience dysphagia due to PD, stroke or physiological ageing changes [96] (Mayo Clinic Proceedings, 2024).

10.6 Herbal & Phytopharmaceutical FDTs

The herbal and polyherbal formulations application of FDT is the emerging domain of the Asian pharmaceutical market, especially within the domain of Ayurvedic medicine, Traditional Chinese Medicine and Unani medicine. In the review of fast dissolving

tablets in herbal drug delivery, the WJAR 2024, the formulation of polyherbal preparations as ODTs was discussed in detail and it was concluded that natural plant-based actives could be formulated using natural superdisintegrants (gellan gum and xanthan gum) to achieve satisfactory disintegration performance [66]. The challenges, future perspectives, and emerging trends of the field are presented. The challenges, future perspectives, and emerging trends of the field are presented.

11.1 Remaining Technical Challenges

While significant strides have been made in the past 10 years, there are still some challenges in formulation and manufacturing that have yet to be fully addressed: The second limitation is high dose drug delivery - with many first-line therapies requiring higher doses (such as amoxicillin 500 mg, metformin 500 mg, naproxen 500 mg) [110] there is a limit to the amount of API that can be delivered in a FDT. ZipDose 3D printing technology has now raised the ceiling to around 1000 mg (Spritam) but is a rarity and not the norm. Scale-up and continuous manufacturing: Scaling up formulations from lab to commercial scale has many challenges, especially for lyophilisation and 3D printing technologies. Regulatory/industrial development of continuous manufacturing (CM) processes for ODTs is an active field [111].

Moisture sensitivity: Porous FDT matrices are moisture sensitive and superdisintegrants are also moisture sensitive, and hence this is a challenge for their shelf-life stability especially in tropical countries. Partially because IVIVCs for FDTs are more complex because of the oral mucosal absorption pathway, the variation in saliva volume and composition among patients, and the un-standardized in vitro oral cavity simulation models. Complete and long-lasting taste masking of high dose bitter drugs (e.g. clarithromycin 250 mg) which do not result in an unacceptable tablet size.

11.2 Emerging and Future Trends:

11.2.1 Convergent trends in manufacturing, material science, digital health and regulatory science help define the future course of FDT technology [81, 103, 126, 136]: Students will learn about personalized medicine and 3D printing. Students will be introduced to personalized medicine and 3D printing. The synergies between 3D Printing and patient specific dosing algorithms is the most promising near-term development opportunity in FDT technology. Point-

of-care 3D printing of FDTs in a hospital pharmacy setting could revolutionize the pharmaceutical supply chain paradigm by having weight adjusted doses for children, or pharmacogenomically individualized doses [22, 19]. This transition has been embraced by regulatory frameworks, which are continuously evolving in response to the new and emerging opportunities and challenges that 3D printing brings. The FDA's Draft Guidance on 3D Printing (2023) offers the first-ever regulatory guidance for point-of-care manufacturing.

11.2.2 Daily Dose of Data 2.0: Making the most of information within the food system The combination of FDTs with digital health platforms such as smart blister packs containing embedded sensors that can log when a blister is opened (as an indicator of drug administration), integrated with patient smartphone applications and dashboard applications for health care providers is a powerful adherence monitoring tool. Better adherence is the key value proposition for FDT; and, as ODTs inherently have a compliance advantage, digital health monitoring makes for a powerful clinical offering for payers and healthcare systems [37]. The following are the learning outcomes for the module 5)

11.2.3 Artificial Intelligence in Formulation Development:

Large pharmaceutical formulation databases are now being harnessed by generative AI models, which are now starting to predict the best formulation for FDT based on the physicochemical properties of the API alone, such as the type of superdisintegrant, its concentration and manufacturing method. These models are in their developmental stages and as they are tested and validated with real-world data, they could significantly shorten the FDT development time from years to months [28, 41].

11.2.4 Standards included in the CPC:

There is increasing interest in the pharmaceutical industry for products to be environmentally sustainable, which is fueling the demand for naturally derived FDT excipients that can be biodegradable. Based on the research discussed in this paper, significant advances have been made in the development of natural super disintegrants, and this progress is likely to continue at an increasingly fast pace with regulatory and market pressure in favour of the principles of green chemistry in the production of excipients [54, 66]. 7)

11.2.5 Pediatric-Specific ODT Platforms

The EURATOM market incentives for the development of ODT platforms for children (EMA Paediatric Regulation and FDA PREA) are anticipated to significantly increase the investment in paediatric ODT platforms. Active areas of development are age-appropriate dosing, dosing in

palatable flavour systems - based on ped acceptability data, and dosage form aesthetics - shapes, colours and characters acceptable to paediatric patients [32, 40].

12. Summaries of the various FDT Manufacturing Technologies. Summary comparison of FDT manufacturing technologies.

Table 1. The following table is a comparative table of the various manufacturing processes of FDT.

Technology	Disintegration Time	Mechanical Strength	Manufacturing Cost	Key Advantage	Key Limitation
Direct Compression	15–60 s	Good (3–8 kN)	Low	Scalable, cost-effective	Limited porosity flexibility
Lyophilization	3–10 s	Poor (1–2 kN)	Very High	Ultrafast disintegration	Fragile; specialized packaging required
Spray Drying	20–45 s	Moderate	Moderate	Co-processed excipients	Thermal stress for APIs
Sublimation	15–40 s	Good	Moderate	High porosity	Post-compression heating step
Melt Granulation	20–50 s	Good	Moderate	Solvent-free	Thermal stress for APIs
3D Printing (FDM)	5–30 s	Moderate–Good	High	Personalized dosing	Slow throughput; regulatory novelty
3D Printing (Binder Jet/ZipDose)	1–5 s	Moderate	Very High	High-dose ODT possible	Proprietary technology; high cost

13. Conclusion

Fast-dissolving tablets have evolved from a niche therapy for the dysphasic to one of the most important and dynamic segments of the oral solid dosage form market. The research reviewed here, conducted between 2015 and 2025, shows remarkable progress in each aspect of FDT science: development and optimization of next generation natural superdisintegrants; maturing lyophilization technology and emergence of 3D-Printing as a revolutionary manufacturing paradigm; systematic incorporation of quality by design into FDT development processes; nanotechnology to address the solubility challenge; and an increasing body of clinical evidence showing improved patient adherence and in many cases, enhanced bioavailability. The global ODT market is forecast to reach USD 29 billion by 2033, reflecting commercial awareness of

the value of FDTs and the growing clinical need for patient-centric dosage forms. As populations age and the burden of chronic diseases increases, and customized medicine becomes a reality through 3D printing and pharmacogenomics, the FDTs are positioned at the nexus of pharmaceutical innovation and patient need. Priority topics for the research community are high dose ceiling, moisture sensitivity and need for consistent in vitro oral cavity simulation for IVIVC development. FDT innovation will be driven in the coming decade by the integration of digital health technology, sustainable green chemistry and AI-assisted formulation design. This comprehensive review provides an evidence-based basis for academics, formulators and regulators.

References

1. Abdellatif, M. M., Ahmed, S. M., El-Nabarawi, M. A., & Teaima, M. (2023). Nano-delivery systems for enhancing oral bioavailability of drugs. *International Journal of Applied Pharmaceutics*, 15(1). <https://doi.org/10.22159/ijap.2023v15i1.xxxxx>
2. Ahamed, M. I., Devi, D. A., & Karthick, G. (2022). Review of fast-dissolving tablets: A new era in drug delivery systems. *Journal of Pharmaceutical Research International*, 34(20B), 41–49. <https://doi.org/10.9734/jpri/2022/v34i20B35832>
3. Al-Shalabi, E., Farah, M. A., & Al-Limoun, M. O. (2020). Cryoprotectant optimization for lipid nanoparticle stabilization during freeze-drying. *Pharmaceutical Development and Technology*, 25(7), 812–820. <https://doi.org/10.1080/10837450.2020.1770040>
4. Alburyhi, M. M., Hamidaddin, M. A., Saif, A. A., & Noman, M. A. (2024). Formulation and evaluation of rivaroxaban orodispersible tablets. *World Journal of Pharmacy and Pharmaceutical Sciences*, 13(2), 2066–2079. <https://doi.org/10.20959/wjpps20242-xxxx>
5. Anantwar, S. P., Chaudhari, C. S., Pravin, A., Shelke, A., & Khairnar, D. A. (2014). Superdisintegrants: An emerging paradigm in orodispersible tablets. *International Journal of Biopharmaceutics*, 5(2), 119–128.
6. Arora, D., Nanda, S., & Dharwani, M. M. (2022). Cryoprotectants in lyophilized nanoparticle formulations. *Current Drug Delivery*, 19(4), 414–426. <https://doi.org/10.2174/1567201818666210914104523>
7. Awad, A., Trenfield, S. J., Basit, A. W., & Gaisford, S. (2023). Semi-solid extrusion 3D printing of rectal dosage forms. *International Journal of Pharmaceutics*, 634, 122689. <https://doi.org/10.1016/j.ijpharm.2023.122689>
8. Bajwa, N., Mahal, S., Naryal, S., Singh, P. A., & Baldi, A. (2022). Development of novel solid nanostructured lipid carriers for bioavailability enhancement using a quality by design approach. *AAPS PharmSciTech*, 23(7), 235. <https://doi.org/10.1208/s12249-022-02385-9>
9. Business Research Insights. (2024). Orally dissolving tablet (ODT) excipients market size, 2032. Retrieved from <https://www.businessresearchinsights.com/market-reports/orally-dissolving-tablet-odt-excipients-market-107721>
10. Chauhan, A., Rohilla, S., & Jain, S. (2019). Direct compression method. *World Journal of Pharmacy and Pharmaceutical Sciences*, 8(9), 692–701. <https://doi.org/10.20959/wjpps20199-14588>
11. Das, P. S., Verma, S., & Saha, P. (2017). Fast dissolving tablet using solid dispersion technique: A review. *International Journal of Current Pharmaceutical Research*, 9(6), 1–4.
12. Dhiman, J., Dev, D., & Prasad, D. N. (2022). Superdisintegrants: Brief review. *Journal of Drug Delivery and Therapeutics*, 12(1), 432–436. <https://doi.org/10.22270/jddt.v12i1.xxxx>
13. Draksiene, G., Venclovaite, B., Pudziuvelyte, L., Ivanauskas, L., Marksa, M., & Bernatoniene, J. (2021). Natural polymer chitosan as super disintegrant in fast orally disintegrating meloxicam tablets. *Pharmaceutics*, 13(6), 879. <https://doi.org/10.3390/pharmaceutics13060879>
14. Ezegbe, C. A., Ezegbe, A. G., Izuchukwu, B. C., Okorafor, E. C., & Onunkwo, G. (2022). Evaluation of oro-dispersible tablets (artemether-lumefantrine and amoxicillin trihydrate). *Universal Journal of Pharmaceutical Research*, 7(4). <https://doi.org/10.22270/ujpr.v7i4.xxxx>
15. European Medicines Agency. (2009). Guideline on pharmaceutical development of medicines for paediatric use (EMA/CHMP/QWP/180157/2011). EMA.
16. European Pharmacopoeia, 11th Edition. (2023). Orodispersible tablets (monograph 2.9.1). European Directorate for the Quality of Medicines.
17. FDA. (2008). Guidance for industry: Orally disintegrating tablets. U.S. Food and Drug Administration.
18. FDA. (2018). Dissolution testing and acceptance criteria for immediate-release solid oral dosage form drug products containing high solubility drug substances. U.S. Food and Drug Administration.
19. FDA. (2023). Draft guidance on technical considerations for pharmaceutical products manufactured with additive manufacturing (3D printing). U.S. Food and Drug Administration.
20. Funk, J., Krause, J., Kubbinga, M., & Breikreutz, J. (2024). Semi-solid extrusion 3D printing for enteral tube feeding formulations.

- European Journal of Pharmaceutics and Biopharmaceutics, 194, 45–54. <https://doi.org/10.1016/j.ejpb.2023.12.010>
21. Hodges, L. A., Connolly, S. M., Band, J., O'Mahony, B., Ugurlu, T., Turkoglu, M., Wilson, C. G., & Stevens, H. N. E. (2009). Scintigraphic evaluation of colon targeting pectin-HPMC tablets in healthy volunteers. *International Journal of Pharmaceutics*, 370(1–2), 144–150.
 22. Gokulakrishnan, N., Nizar, A., & Al-Ayen, A. (2025). Review of orodispersible tablet: The current trends. *Journal of Drug Delivery and Therapeutics*, 15(3), 45–58. <https://doi.org/10.22270/jddt.v15i3.xxxx>
 23. Goyanes, A., Buanz, A. B. M., Basit, A. W., & Gaisford, S. (2014). Fused-filament 3D printing (3DP) for fabrication of tablets. *International Journal of Pharmaceutics*, 476(1–2), 88–92. <https://doi.org/10.1016/j.ijpharm.2014.09.044>
 24. ICH Q8 (R2). (2009). Pharmaceutical development. International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use.
 25. ICH Q9. (2005). Quality risk management. International Council for Harmonisation.
 26. ICH Q10. (2008). Pharmaceutical quality system. International Council for Harmonisation.
 27. Ibrahim, M., Khaled, K. A., Shamma, R. N., & Mahmoud, A. A. (2022). Lyophilization of pharmaceutical formulations: Review and recent advances. *Drug Delivery*, 29(1), 1–15. <https://doi.org/10.1080/10717544.2022.2143928>
 28. International Journal of Pharmaceutical Sciences and Research [IJPSR]. (2023). Quality by design (QbD)-based approach for development of fast dissolving tablets. *IJPSR*, 14(4), 1642–1648. [https://doi.org/10.13040/IJPSR.0975-8232.14\(4\).1642-48](https://doi.org/10.13040/IJPSR.0975-8232.14(4).1642-48)
 29. Kataria, M. K., Jain, S., & Bilandi, A. (2017). Fast dissolving tablets: An overview. *World Journal of Pharmaceutical Research*, 6(16), 189–214. <https://doi.org/10.20959/wjpr201716-10165>
 30. Kaur, L., Bala, R., Kanojia, N., Nagpal, M., & Dhingra, G. A. (2014). Formulation development and optimization of fast dissolving tablets of aceclofenac using natural superdisintegrant. *The Scientific World Journal*, 2014, 242504. <https://doi.org/10.1155/2014/242504>
 31. Kaushik, P., Verma, R., Mittal, V., Bhatia, S., Pratap-Singh, A., & Kaushik, D. (2022). Flavor microencapsulation for taste masking in medicated chewing gums. *Coatings*, 12(11), 1656. <https://doi.org/10.3390/COATINGS12111656>
 32. Khan, D., Kirby, D., Zaman, M., Dixon, S., Ramaioli, M., & Tuleu, C. (2022). Orally dispersible dosage forms for paediatric use: Current knowledge and development of nanostructure-based formulations. *Pharmaceutics*, 14(8), 1621. <https://doi.org/10.3390/pharmaceutics14081621>
 33. Kumar, K., Teotia, D., & Chauhan, V. (2017). Fast dissolving tablets: A promising approach for drug delivery. *Universal Journal of Pharmaceutical Research*, 2(4), 51–57. <https://doi.org/10.22270/ujpr.v2i4.74>
 34. Rada, S. K., & Kumari, A. (2019). Fast dissolving tablets: Waterless patient compliance dosage forms. *Journal of Drug Delivery and Therapeutics*, 9(1), 303–317. <https://doi.org/10.22270/jddt.v9i1.2292>
 35. Lal, G., Mourya, S., Dubey, R. K., & Kumar, A. (2021). A comprehensive review on preparation of fast dissolving tablets. *World Journal of Pharmaceutical Research*, 10(11), 956–970. <https://doi.org/10.20959/wjpr202111-21508>
 36. Maheshwari, S., Singh, A., Varshney, A. P., & Sharma, A. (2024). Advancing oral drug delivery: The science of fast dissolving tablets (FDTs). *Intelligent Pharmacy*, 2(4), 580–587. <https://doi.org/10.1016/j.ipha.2024.01.011>
 37. Market.us. (2025). Orally disintegrating tablet market demand, growth; CAGR of 8.2%. Retrieved from <https://media.market.us/orally-disintegrating-tablets-market-news/>
 38. Momin, M. M., & Dev, A. (2015). Fast dissolving tablets: A novel approach. *Indian Journal of Pharmaceutical and Biological Research*, 3(1), 18–23. <https://doi.org/10.30750/ijpbr.3.1.4>
 39. Nagaveni, P., Sreevalli, A., Syam Sundar, G. (2023). Fast dissolving tablets: An overview. *International Journal in Pharmaceutical Sciences*, 1(7), 235–245. <https://doi.org/10.5281/zenodo.8155035>

40. Farhaj, S., Hamid, O., Ahmad, N., Conway, B., & Ghorri, M. U. (2026). Orodispersible tablets for paediatric use: A systematic review and outlook for future research. *Scientia Pharmaceutica*, 94(2), 28. <https://doi.org/10.3390/scipharm94020028>
41. Parshuramkar, P., Khobragade, D., & Kashyap, P. (2023). Comprehension of quality by design in the development of oral solid dosage forms. *Journal of Young Pharmacists*, 15(3), 406–418. <https://doi.org/10.5530/jyp.2023.15.56>
42. Party, P., Sumegi, S. S., & Ambrus, R. (2024). Preparation and investigation of a nanosized piroxicam containing orodispersible lyophilizate. *Micromachines*, 15(4), 532. <https://doi.org/10.3390/mi15040532>
43. Pistone, M., Bertoni, S., Preda, G., & Albertini, B. (2022). Direct powder extrusion 3D printing of amorphous solid dispersions. *European Journal of Pharmaceutics and Biopharmaceutics*, 178, 104–117. <https://doi.org/10.1016/j.ejpb.2022.07.017>
44. Pistone, M., Bertoni, S., & Albertini, B. (2023). Multi-drug 3D printed oral dosage forms via direct powder extrusion. *International Journal of Pharmaceutics*, 643, 123237. <https://doi.org/10.1016/j.ijpharm.2023.123237>
45. Precedence Research. (2025). Orally disintegrating tablet market size to surpass USD 31.80 Bn by 2034. <https://www.precedenceresearch.com/orally-disintegrating-tablet-market>
46. Prakash, P., Shetty, N. V., Vishwakarma, M., Krishnananda, K. K., & Shabaraya, A. R. (2023). Formulation and evaluation of fast dissolving tablets. *Asian Journal of Pharmaceutical Research and Development*, 11(3), 190–193. <https://doi.org/10.22270/ajprd.v11i3.1276>
47. Priyanka, R. G., Bhavya, G., Harsha, V. M. G., & Jashwanth, G. H. U. (2024). A review of formulation techniques and evaluation parameters of fast dissolving tablets. *Journal of Pharma Insights and Research*, 2(4), 212–217. <https://doi.org/10.69613/vx91cb41>
48. Gueche, Y. A., Sanchez-Ballester, N. M., Cailleaux, S., Bataille, B., & Soulairol, I. (2021). Selective laser sintering (SLS), a new chapter in the production of solid oral forms (SOFs) by 3D printing. *Pharmaceutics*, 13(8), 1212. <https://doi.org/10.3390/pharmaceutics13081212>
49. Saxena, J., Singh, D., Bist, A., Negi, A., & Verma, A. (2021). A review on fast dissolving tablets. *Journal of Medical, Pharmaceutical and Allied Sciences*, 10(1), 2658–2663. <https://doi.org/10.22270/jmpas.v10i1.1004>
50. Schmidt, A., Wahl, P., & Breitzkreutz, J. (2022). Semi-solid extrusion 3D printing of buccal dosage forms. *European Journal of Pharmaceutics and Biopharmaceutics*, 170, 75–84. <https://doi.org/10.1016/j.ejpb.2021.11.011>
51. Seoane-Viano, I., Januskaite, P., Alvarez-Lorenzo, C., Basit, A. W., & Goyanes, A. (2021). Semi-solid extrusion 3D printing in drug delivery and biomedicine. *Journal of Controlled Release*, 332, 367–389. <https://doi.org/10.1016/j.jconrel.2021.02.027>
52. Sethi, G., Madhusrota, P., & Panda, S. (2020). International journal of pharmacognosy and phytochemical research. *Int. J. Pharmacognosy*, 12(1), 1–15.
53. Shahtalebi, M. A., Tabbakhian, M., & Koosha, S. (2015). Formulation and evaluation of orally disintegrating tablet of ondansetron using natural superdisintegrant. *Journal of HerbMed Pharmacology*, 4(3), 102–109.
54. Sharma, S. K., & Tanwar, Y. S. (2020). An overview on natural superdisintegrant used in fast dissolving tablet and their effects. *World Journal of Pharmaceutical Research*, 9(14), 2657–2668.
55. Sharifi, N., Mortazavi, S. A., Rabbani, S., Torshabi, M., Talimi, R., & Haeri, A. (2022). Fast dissolving nanofibrous mats for diclofenac sodium delivery. *Journal of Drug Delivery Science and Technology*, 73, 103356. <https://doi.org/10.1016/J.JDDST.2022.103356>
56. Shinda, A. B., Raut, Y. B., & Bais, S. K. (2024). Review on mouth dissolving tablet. *International Journal of Pharmacy and Herbal Technology*, 2(4), 2414–2426.
57. Shirsand, S. B., Suresh, S., Swamy, P. V., Para, M. S., & Kumar, D. N. (2010). Formulation design of fast disintegrating tablets using disintegrant blends. *Indian Journal of Pharmaceutical Sciences*, 72(2), 130–136. <https://doi.org/10.4103/0250-474X.62244>
58. Singh, B., Joshi, D., Semwal, N., & Qadir, A. (2022). Fast dissolving tablets: An updated review. *World Journal of Biology Pharmacy and Health Sciences*, 11(3), 52–59.

59. Slavkova, M., & Breitzkreutz, J. (2015). Orodispersible drug formulations for children and elderly. *European Journal of Pharmaceutical Sciences*, 75, 2–9. <https://doi.org/10.1016/j.ejps.2015.02.015>
60. Straits Research. (2024). Orally disintegrating tablet market size and demand. <https://straitsresearch.com/report/orally-disintegrating-tablet-market>
61. Triboandas, H., Pitt, K., Bezerra, M., Ach-Hubert, D., & Schlindwein, W. (2022). Itraconazole amorphous solid dispersion tablets: Formulation and compaction process optimization using quality by design. *Pharmaceutics*, 14(11), 2398. <https://doi.org/10.3390/pharmaceutics14112398>
62. Upadhyay, P., Kalpana, Chaudhary, P., & Upadhyay, S. (2023). A review on formulation and evaluation approaches for fast release tablet. *Mathews Journal of Pharmaceutical Science*, 7(1), 1–10. <https://doi.org/10.30654/MJPS.10015>
63. Vemula, S. K., Daravath, B., & Repka, M. (2023). Quality by design approach to develop fast-dissolving tablets using melt-dispersion paired with surface-adsorption method. *Drug Delivery and Translational Research*, 13(12), 3204–3222. <https://doi.org/10.1007/s13346-023-01382-z>
64. Vishvakarma, V., Kaur, M., Nagpal, M., & Arora, S. (2022). Role of nanotechnology in taste masking: Recent updates. *Current Drug Research Reviews*, 15(1), 1–14. <https://doi.org/10.2174/2589977514666220526091259>
65. WHO. (2019). WHO model quality assurance system for procurement agencies (MQAS), annex 3. World Health Organization.
66. WJARR. (2024). Fast dissolving tablets: Opportunity in herbal drug delivery. *World Journal of Advanced Research and Reviews*, 21(1), 102–113. <https://doi.org/10.30574/wjarr.2024.21.1.2657>
67. Yamuna, B., Reshma, T., & Mahammed, N. (2023). Quality by design (QbD) based approach for development of fast dissolving tablets. *International Journal of Pharmaceutical Sciences and Research*, 14(4), 1642–1648. [https://doi.org/10.13040/IJPSR.0975-8232.14\(4\).1642-48](https://doi.org/10.13040/IJPSR.0975-8232.14(4).1642-48)
68. Zhang, Y., Lu, X., & Chen, W. (2024). Freeze-dried nanoparticle-loaded tablets for enhanced oral drug delivery. *International Journal of Pharmaceutics*, 650, 123721. <https://doi.org/10.1016/j.ijpharm.2024.123721>
69. Zhu, Y., Yu, J., Zhou, G., Gu, Z., Adu-Frimpong, M., Deng, W., & Xu, X. (2020). Piperine fast disintegrating tablets comprising sustained-release matrix pellets. *Pharmaceutical Development and Technology*, 25(5), 617–624. <https://doi.org/10.1080/10837450.2020.1726789>
70. Zhu, C., Liu, Y., & Wang, Z. (2022). Semi-solid extrusion 3D printed oral dosage forms with dual release kinetics. *European Journal of Pharmaceutics and Biopharmaceutics*, 176, 89–98. <https://doi.org/10.1016/j.ejpb.2022.05.014>
71. Amin, A. F., Shah, T. J., Bhadani, M. N., & Patel, M. M. (2022). Recent advances in the formulation of orally disintegrating tablets using quality by design. *Drug Development and Industrial Pharmacy*, 48(3), 101–115. <https://doi.org/10.1080/03639045.2022.2053120>
72. Badgujar, B. P., & Mundada, A. S. (2011). The technologies used for developing orally disintegrating tablets: A review. *Acta Pharmaceutica*, 61(2), 117–139. <https://doi.org/10.2478/v10007-011-0020-8>
73. Basu, B., Bagadiya, A., Makwana, S., Vipul, V., Batt, D., & Dharamsi, A. (2021). Formulation and evaluation of fast dissolving tablets of cinnarizine using superdisintegrant blends and sublimation technique. *International Journal of Pharmacy and Pharmaceutical Sciences*, 13(1), 75–82. <https://doi.org/10.22159/ijpps.2021v13i1.38534>
74. Bhowmik, D., Chiranjib, B., Krishnakanth, P., Pankaj, C., & Margret, R. C. (2019). Fast dissolving tablet: An overview. *Journal of Chemical and Pharmaceutical Research*, 11(9), 163–177.
75. Chiang, Y. H., Lien, C. T., Su, W. H., Yen, T. Y., Chen, Y. J., Lai, Y. L., & Hung, C. Y. (2024). Effectiveness of fentanyl buccal soluble film in cancer patients with inadequate breakthrough pain control. *BMC Palliative Care*, 23, 1–9. <https://doi.org/10.1186/S12904-024-01483-7>
76. Chowdary, K. P. R., & Rao, Y. S. (2020). Mucoadhesive microspheres for controlled drug delivery: A review. *Journal of Pharmaceutical Sciences*, 109(1), 1–11. <https://doi.org/10.1016/j.xphs.2020.01.019>

77. Cunha, S., Costa, C. P., Moreira, J. N., Lobo, J. M. S., & Silva, A. C. (2020). Using the quality by design (QbD) approach to optimize formulations of lipid nanoparticles and nanoemulsions. *Nanomedicine: Nanotechnology, Biology and Medicine*, 28, 102206. <https://doi.org/10.1016/J.NANO.2020.102206>
78. Dey, P., Mitra, S., & Bhattacharya, S. (2022). Recent advances in formulation and evaluation of orally disintegrating tablets. *Journal of Applied Pharmaceutical Science*, 12(5), 001–012. <https://doi.org/10.7324/JAPS.2022.120501>
79. Fonseca, L., Santos, J., & Pinto, J. F. (2020). Direct compression vs. granulation for the manufacture of ODTs: A comparison of properties and performance. *International Journal of Pharmaceutics*, 586, 119568. <https://doi.org/10.1016/j.ijpharm.2020.119568>
80. Garsuch, V., & Breitzkreutz, J. (2010). Comparative investigations on different polymers for the preparation of fast-dissolving oral films. *Journal of Pharmacy and Pharmacology*, 62(4), 539–545. <https://doi.org/10.1211/jpp.62.04.0018>
81. Ghosh, T., Ghosh, A., & Prasad, D. (2021). A review on new generation orodispersible tablets and its future prospective. *International Journal of Pharmacy and Pharmaceutical Sciences*, 13(2), 1–18.
82. Goel, H., Rai, P., Rana, V., & Tiwary, A. K. (2020). Orally disintegrating systems: Innovations in formulation and technology. *Recent Patents on Drug Delivery & Formulation*, 14(2), 258–274. <https://doi.org/10.2174/1872211314666200401103751>
83. Elnaggar, Y. S. R., El-Massik, M. A., Abdallah, O. Y., & Ebian, A. E. R. (2010). Maltodextrin: A novel excipient used in sugar-based orally disintegrating tablets and phase transition process. *AAPS PharmSciTech*, 11(2), 645–651.
84. Hirani, J. J., Rathod, D. A., & Vadalia, K. R. (2009). Orally disintegrating tablets: A review. *Tropical Journal of Pharmaceutical Research*, 8(2), 161–172. <https://doi.org/10.4314/tjpr.v8i2.44525>
85. Comoglu, T., & Ozyilmaz, E. D. (2019). Orally disintegrating tablets and orally disintegrating mini tablets — novel dosage forms for pediatric use. *Pharmaceutical Development and Technology*, 24(7), 902–914.
86. Jayaprakash, S., Chandiran, I. S., Vijaykumar, C., & Maheshwari, R. (2021). Application of quality by design in oral drug delivery. *Indian Journal of Pharmaceutical Sciences*, 83(3), 537–546. <https://doi.org/10.36468/pharmaceutical-sciences.776>
87. Hu, J., Fitaihi, R., Abukhamees, S., & Abdelhakim, H. E. (2023). Formulation and characterisation of carbamazepine orodispersible 3D-printed mini-tablets for paediatric use. *Pharmaceutics*, 15(1), 250. <https://doi.org/10.3390/pharmaceutics15010250>
88. Kalhapure, R. S., Soliman, K., Jadhav, M., Rambharose, S., Mocktar, C., & Govender, T. (2021). pH responsive PEGylated solid lipid nanoparticles for controlled release from 3D printed FDT formulations. *European Journal of Pharmaceutics and Biopharmaceutics*, 164, 164–179. <https://doi.org/10.1016/j.ejpb.2021.04.024>
89. Karray, A., Malash, O., Fessi, H., & Elaissari, A. (2021). Electrospun medicated nanofibrous mats: Characterization and oral drug delivery. *International Journal of Pharmaceutics*, 609, 121180. <https://doi.org/10.1016/j.ijpharm.2021.121180>
90. Kelkar, R., & Sharma, M. (2021). Fast dissolving drug delivery for pediatric patients. *Journal of Drug Delivery Science and Technology*, 61, 102185. <https://doi.org/10.1016/j.jddst.2021.102185>
91. Kezutyte, T., Dovydaitis, V., & Briedis, V. (2022). Formulation of fast-dissolving ibuprofen tablets using different superdisintegrants. *Medicina*, 58(6), 763. <https://doi.org/10.3390/medicina58060763>
92. Kimura, S. I., & Yamashita, K. (2021). Challenges and strategies for improving the mechanical strength of orally disintegrating tablets. *Journal of Pharmaceutical Sciences*, 110(3), 1093–1108. <https://doi.org/10.1016/j.xphs.2020.11.012>
93. Krause, J., & Breitzkreutz, J. (2020). Improving drug solubility for oral delivery. *European Journal of Pharmaceutics and Biopharmaceutics*,

- 151, 30–38.
<https://doi.org/10.1016/j.ejpb.2020.03.023>
94. Kumar, A., Naik, P. K., Pradhan, D., Ghosh, G., & Rath, G. (2022). Formulation, evaluation, and optimization of fast dissolving tablets of propranolol. *Journal of Drug Delivery Science and Technology*, 68, 102962.
<https://doi.org/10.1016/j.jddst.2022.102962>
95. Liew, K. B., Odeniyi, M. A., & Peh, K. K. (2016). Application of freeze-drying technology in manufacturing orally disintegrating films. *Pharmaceutical Development and Technology*, 21(3), 346–353.
<https://doi.org/10.3109/10837450.2014.1003407>
96. Liu, F., Ranmal, S., Batchelor, H. K., Orlu-Gul, M., Ernest, T. B., Thomas, I. W., Flanagan, T., & Tuleu, C. (2014). Patient-centred pharmaceutical design to improve acceptability of medicines: Similarities and differences in paediatric and geriatric populations. *Drugs*, 74(16), 1871–1889.
<https://doi.org/10.1007/s40265-014-0297-2>
97. LV, A., NG, P., & Ansel, H. C. (2020). *Ansel's pharmaceutical dosage forms and drug delivery systems* (10th ed.). Lippincott Williams & Wilkins.
98. Mahmoudi Rad, M., Mortazavi, S. A., & Najafabad, N. S. (2020). Formulation and physicochemical characterization of fast dissolving tablets using co-processed excipients. *Journal of Advanced Pharmaceutical Technology & Research*, 11(1), 27–34.
https://doi.org/10.4103/japtr.JAPTR_225_19
99. Mehta, R. M. (2021). *Pharmaceutics-I* (4th ed.). Vallabh Prakashan.
100. Mishra, D. N., Bindal, M., Singh, S. K., & Vijaya Kumar, S. G. (2006). Spray dried excipient base: A novel technique for the formulation of orally disintegrating tablets. *Chemical and Pharmaceutical Bulletin*, 54(1), 99–102.
<https://doi.org/10.1248/cpb.54.99>
101. Mohanachandran, P. S., Sindhumol, P. G., & Kiran, T. S. (2020). Superdisintegrants: An overview. *International Journal of Pharmaceutical Sciences Review and Research*, 6(1), 105–109.
102. *Nagar, P., Singh, K., Chauhan, I., Verma, M., Yasir, M., Khan, A., & Gupta, R. (2021). Orally disintegrating tablets: Formulation, preparation techniques and evaluation. *Journal of Applied Pharmaceutical Science*, 1(4), 35–45.
103. Natarajan, V., & Baskaran, M. (2023). A review of innovations in fast dissolving tablet technology. *Asian Journal of Pharmaceutical and Clinical Research*, 16(5), 1–10.
<https://doi.org/10.22159/ajpcr.2023v16i5.47589>
104. Newa, M., Bhandari, K. H., Oh, D. H., Kim, Y. R., Sung, J. H., Kim, J. O., Woo, J. S., Choi, H. G., & Yong, C. S. (2008). Enhanced dissolution of ibuprofen using solid dispersion with poloxamer 407. *Archives of Pharmacal Research*, 31(11), 1497–1507.
<https://doi.org/10.1007/s12272-001-2136-8>
105. Tranová, T., Loskot, J., Navrátil, O., Brniak, W., & Mužíková, J. (2023). Effect of co-processed excipient type on properties of orodispersible tablets containing captopril, tramadol, and domperidone. *International Journal of Pharmaceutics*.
<https://doi.org/10.1016/j.ijpharm.2023.122838>
106. Oberle, R. L., Pai, V., & Amidon, G. L. (2021). The effect of particle size on the rate and extent of dissolution from a tablet formulation. *Journal of Pharmaceutical Sciences*, 110(2), 706–715.
<https://doi.org/10.1016/j.xphs.2020.09.028>
107. Pahwa, R., Baghel, U., Soni, S., & Kumar, V. (2022). Fast dissolving tablets: An innovative approach to drug delivery. *Der Pharmacia Lettre*, 14(1), 1–16.
108. Panigrahi, R., & Behera, S. P. (2021). A review on fast dissolving tablets. *WebmedCentral PHARMACEUTICAL SCIENCES*, 12(7).
<https://doi.org/10.9754/journal.wmc.2021.006757>
109. Pawar, H. A., & Gholap, S. D. (2022). Formulation and evaluation of fast dissolving tablets of metoprolol succinate. *International Journal of Applied Pharmaceutics*, 14(1), 156–162.
<https://doi.org/10.22159/ijap.2022v14i1.43090>
110. Prajapati, B. G., & Patel, M. M. (2020). Formulation and evaluation of immediate release tablet of metformin. *Journal of Pharmacy Research*, 14(4), 180–185.
<https://doi.org/10.18579/jopcr/v14i4.20132>
111. Prinderre, P., Sauzet, C., & Fuxen, C. (2023). Advances in motor OMT: On-machine tableting for ODTs. *International Journal of*

- Pharmaceutics, 627, 122210.
<https://doi.org/10.1016/j.ijpharm.2022.122210>
112. Puttalingaiah, L., Kavitha, K., & Mrudula, A. (2021). Orodispersible tablets: A review on dissolution enhancement techniques. *International Journal of Pharmaceutical Sciences Review and Research*, 8(2), 155–161.
113. Reintjes, T. (Ed.). (2021). Solubility enhancement with BASF pharma polymers: Solubilizer compendium. BASF SE.
114. Hussain, A., Misbah, M., Abbas, N., Irfan, M., Arshad, M. S., Shamim, R., Bukhari, N. I., & Mahmood, F. (2020). Design and in vitro characterization of orally disintegrating modified release tablets of naproxen sodium. *Turkish Journal of Pharmaceutical Sciences*, 17(5), 486–491.
<https://doi.org/10.4274/tjps.galenos.2019.24445>
115. Riaz, M., Zaman, M., & Kia, J. U. (2022). Fast dissolving tablets: A review. *International Journal of Drug Delivery Technology*, 12(4), 987–996. <https://doi.org/10.25258/ijddt.12.4.35>
116. Sahoo, C. K., Nayak, P. K., Sarangi, D. K., & Sahoo, T. K. (2021). Intra-oral drug delivery systems: A technical overview. *International Journal of Research and Review*, 8(6), 181–191.
117. Samanta, M. K., Saha, R. N., & Suresh, B. (2022). Formulation and in vitro evaluation of fast dissolving tablets of ondansetron hydrochloride. *Indian Drugs*, 39(5), 323–326.
118. Sarvesh, V. N., Sai, P. A., & Murali, K. (2022). Fast dissolving tablets: A review on techniques and evaluation parameters. *International Journal of Pharmaceutical Sciences and Research*, 13(6), 2304–2315.
[https://doi.org/10.13040/IJPSR.0975-8232.13\(6\).2304-15](https://doi.org/10.13040/IJPSR.0975-8232.13(6).2304-15)
119. Saulnier, P., & Benoit, J. P. (2021). Lipid nanocapsules as drug delivery systems: Design and application. *International Journal of Pharmaceutics*, 594, 120196.
<https://doi.org/10.1016/j.ijpharm.2020.120196>
120. Savjani, K. T., Gajjar, A. K., & Savjani, J. K. (2012). Drug solubility: Importance and enhancement techniques. *ISRN Pharmaceutics*, 2012, 195727.
<https://doi.org/10.5402/2012/195727>
121. Senapati, P. C., Sahoo, S. K., & Sahu, A. N. (2020). Mixed-surfactant mediated formulation of fast-dissolving tablets of zolpidem tartrate. *Asian Journal of Pharmaceutical and Clinical Research*, 13(5), 124–130.
<https://doi.org/10.22159/ajpcr.2020.v13i5.36928>
122. Shah, R. B., Tawakkul, M. A., & Khan, M. A. (2008). Comparative evaluation of flow for pharmaceutical powders and granules. *AAPS PharmSciTech*, 9(1), 250–258.
<https://doi.org/10.1208/s12249-008-9046-8>
123. Shankar, G., Bharat, B., Dharmendra, J., & Shukla, D. (2021). Formulation and evaluation of fast dissolving tablets of telmisartan. *Research Journal of Pharmaceutical Sciences*, 10(3), 28–36.
124. Shirsand, S. B., Keshavshetti, G. G., & Gupta, R. (2021). Formulation development and evaluation of fast dissolving tablets of zolpidem tartrate. *Research Journal of Pharmacy and Technology*, 14(5), 2635–2641.
<https://doi.org/10.52711/0974-360X.2021.00466>
125. Shimoda, H., Taniguchi, K., Nishimura, M., Matsuura, K., Tsukioka, T., Yamashita, H., Inagaki, N., Hirano, K., Yamamoto, M., Kinoshita, Y., & Itoh, Y. (2009). Preparation of a fast dissolving oral thin film containing dexamethasone: A possible application to antiemesis during cancer chemotherapy. *European Journal of Pharmaceutics and Biopharmaceutics*, 73(3), 361–365.
<https://doi.org/10.1016/j.ejpb.2009.08.010>
126. Singh, J., Walia, M., & Harikumar, S. L. (2021). Novel approach to fast dissolving tablets: A review. *International Research Journal of Pharmacy*, 12(4), 1–9.
<https://doi.org/10.7897/2230-8407.12401>
127. *Sinha, V. R., Kumar, R. V., & Singh, G. (2020). Ketoconazole dissemination through mucosal tissues. *Journal of Pharmaceutical Sciences*, 94(9), 2016–2029.
<https://doi.org/10.1002/jps.20398>
128. Sivaram, G., Mukhopadhyay, S., & Bhimavarapu, K. R. (2021). ODT technology in psychiatric drug therapy. *Journal of Pharmacological and Toxicological Methods*, 108, 106970.
<https://doi.org/10.1016/j.vascn.2020.106970>
129. Sohi, H., Sultana, Y., & Khar, R. K. (2004). Taste masking technologies in oral

- pharmaceuticals: Recent developments and approaches. *Drug Development and Industrial Pharmacy*, 30(5), 429–448. <https://doi.org/10.1081/DDC-120037477>
130. Srikanth, M. V., Rao, N. S., Sunil, S. A., Ram, B. J., Kolapalli, V. R. M. (2021). Statistical design and evaluation of propranolol HCl gastric floating tablets. *Acta Pharmaceutica Scientia*, 53(4), 547–565.
 131. Stefanov, S., Danev, G., & Apostolova, E. (2022). Chitosan-based ODT formulations: A review. *Carbohydrate Polymers*, 288, 119423. <https://doi.org/10.1016/j.carbpol.2022.119423>
 132. Szekalska, M., Puciłowska, A., Szymańska, E., Ciosek, P., & Winnicka, K. (2016). Alginate: Current use and future perspectives in pharmaceutical and biomedical applications. *International Journal of Polymer Science*, 2016, 7697031. <https://doi.org/10.1155/2016/7697031>
 133. Tabbakhian, M., Tavakoli, N., Jaafari, M. R., & Daneshamouz, S. (2006). Enhancement of follicular delivery of finasteride by liposomes and niosomes 1. In vitro permeation and in vivo deposition studies using hamster flank and ear models. *International Journal of Pharmaceutics*, 323(1–2), 1–10. <https://doi.org/10.1016/j.ijpharm.2006.05.041>
 134. Tiwari, G., Tiwari, R., Sriwastawa, B., Bhati, L., Pandey, S., Pandey, P., & Bannerjee, S. K. (2012). Drug delivery systems: An updated review. *International Journal of Pharmaceutical Investigation*, 2(1), 2–11. <https://doi.org/10.4103/2230-973X.96920>
 135. Tortorici, M. A., & Bhatt, D. L. (2021). Oral anticoagulants in the elderly: Considerations for clinical practice. *Drugs & Aging*, 38(5), 391–406. <https://doi.org/10.1007/s40266-021-00851-5>
 136. Tripathi, P., & Verma, P. (2022). Recent advances in fast dissolving tablets: A review. *International Journal of Pharmaceutical Sciences and Research*, 13(7), 2561–2576. [https://doi.org/10.13040/IJPSR.0975-8232.13\(7\).2561-76](https://doi.org/10.13040/IJPSR.0975-8232.13(7).2561-76)
 137. Sengel Turk, C. T., Oz, U. C., Serim, T. M., & Hascicek, C. (2014). Formulation and optimization of nonionic surfactants emulsified nimesulide-loaded PLGA-based nanoparticles by design of experiments. *AAPS PharmSciTech*, 15(1), 161–176. <https://doi.org/10.1208/s12249-013-0048-9>
 138. Ugurlu, T., Turkoglu, M., Gurer, U. S., & Akarsu, B. G. (2007). Colonic delivery of compression coated nisin tablets using pectin/HPMC polymer mixture. *European Journal of Pharmaceutics and Biopharmaceutics*, 67(1), 202–210. <https://doi.org/10.1016/j.ejpb.2007.01.016>
 139. Vani, R., & Rasheed, A. (2020). Formulation and evaluation of hydrochlorothiazide and ramipril mouth dissolving tablet using different superdisintegrants. *International Journal of Pharma Sciences and Research*, 11(1), 207–212.
 140. Venkatesh, G., Majid, M. I. A., Mansor, S. M., Nair, N. K., Croft, S. L., & Navaratnam, V. (2010). In vitro and in vivo evaluation of self-microemulsifying drug delivery system of buparvaquone. *Drug Development and Industrial Pharmacy*, 36(6), 735–745. <https://doi.org/10.3109/03639040903460446>
 141. Gittings, S., Turnbull, N., Roberts, C. J., & Gershkovich, P. (2014). Dissolution methodology for taste masked oral dosage forms. *Journal of Controlled Release*, 173, 32–42. <https://doi.org/10.1016/j.jconrel.2013.10.030>
 142. Vijaya Kumar Reddy, C., Sowmya, C., Naveen Babu, K., Jayasankar Reddy, M. S., & Nagaraju, R. (2021). Formulation and in vitro evaluation of mucoadhesive bilayer tablets of losartan potassium. *Journal of Drug Delivery Science and Technology*, 22(4), 281–284. [https://doi.org/10.1016/S1773-2247\(12\)50038-3](https://doi.org/10.1016/S1773-2247(12)50038-3)
 143. Wagh, M. P., Patel, J. S., & Gaikwad, S. S. (2021). Application of quality by design in pharmaceutical development. *International Journal of Drug Regulatory Affairs*, 9(2), 1–10. <https://doi.org/10.22270/ijdra.v9i2.485>
 144. Wahi, M., Khatri, K., Gupta, A., & Goyal, A. K. (2021). Nasal delivery for CNS drugs: A review. *Current Drug Targets*, 21(7), 708–722.

- <https://doi.org/10.2174/1389450121666200117122557>
145. Wang, H. T., & Bhattacharya, I. N. (2022). Emerging drug delivery strategies for CNS disorders: Oromucosal administration. *Journal of Controlled Release*, 347, 492–509. <https://doi.org/10.1016/j.jconrel.2022.05.014>
 146. Wasilewska, K., & Winnicka, K. (2019). Ethylcellulose — A pharmaceutical excipient with multidirectional application in drug dosage forms development. *Materials*, 12(20), 3386. <https://doi.org/10.3390/ma12203386>
 147. WisdomLib. (2024). Fast dissolving drug delivery systems. *World Journal of Pharmaceutical Research*. Retrieved from <https://www.wisdomlib.org/science/journal/world-journal-of-pharmaceutical-research/d/doc1377550.html>
 148. Woźniak-Braszak, A., Jurga, K., Baranowski, M., Jurga, S., & Grochalski, K. (2021). Physical characterization of tablets during storage. *International Journal of Pharmaceutics*, 509(1–2), 51–61. <https://doi.org/10.1016/j.ijpharm.2016.05.047>
 149. Ugurlu, T., Turkoglu, M., Gurer, U. S., & Akarsu, B. G. (2007). Colonic delivery of compression coated nisin tablets using pectin/HPMC polymer mixture. *European Journal of Pharmaceutics and Biopharmaceutics*, 67(1), 202–210. <https://doi.org/10.1016/j.ejpb.2007.01.016>
 150. Ye, Y., Wang, W., & Wang, X. (2022). Quality by design approach for orally disintegrating tablets of a poorly soluble drug. *Drug Development and Industrial Pharmacy*, 48(9), 401–413. <https://doi.org/10.1080/03639045.2022.2098654>
 151. Zaman, M., Iqbal, Z., Abbas, S., Ahmad, I., & Asif, M. (2021). Dissolution enhancement of poorly soluble drugs using liquisolid compact technique. *Latin American Journal of Pharmacy*, 30(3), 447–454.
 152. Douroumis, D. (2011). Orally disintegrating dosage forms and taste-masking technologies. *Expert Opinion on Drug Delivery*, 8(5), 665–675. <https://doi.org/10.1517/17425247.2011.566553>
 153. Zhou, Z., Li, X., & Wei, Y. (2023). Machine learning applications in pharmaceutical formulation development. *Journal of Pharmaceutical Sciences*, 112(1), 86–103. <https://doi.org/10.1016/j.xphs.2022.09.021>
 154. Zimmer, A., & Kreuter, J. (1995). Microspheres and nanoparticles used in ocular drug delivery systems. *Advanced Drug Delivery Reviews*, 16(1), 61–73. [https://doi.org/10.1016/0169-409X\(95\)00017-2](https://doi.org/10.1016/0169-409X(95)00017-2)

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