IJNRD.ORG ISSN : 2456-4184
INTERNATIONAL JOURNAL OF NOVEL RESEARCH AND DEVELOPMENT (IJNRD) | IJNRD.ORG
An International Open Access, Peer-reviewed, Refereed Journal

Advancements in Oro-dispersible Tablet Formulations: A Comprehensive Review of Novel Technologies and Emerging Trends

Rita Soyam, Keshav Hirave*, Swati Malkote, Dnyaneshwar Mokaswad, Kamlesh Wadher, Millind Umekar.

[1]Department of Pharmaceutics, Smt. Kishoritai Bhoyar College of Pharmacy, Kamptee, Nagpur, Maharashtra, India 441002.

Corresponding Author:

Keshav S. Hirave

Department of Pharmaceutics

Smt. Kishoritai Bhoyar College of Pharmacy, Kamptee,

Nagpur, Maharashtra, India 441002.

ABSTRACT

Orodispersible tablets (ODTs) have revolutionized pharmaceutical drug delivery by offering an innovative solution to challenges related to patient compliance, particularly in pediatric and geriatric populations. This review provides a comprehensive exploration of recent advancements in ODT formulations, encompassing novel technologies and emerging trends that have reshaped the landscape of oral medication administration. The review begins by delving into the intricate formulation strategies employed in ODT development, emphasizing the pivotal role of excipients, disintegration agents, and superdisintegrants in achieving rapid disintegration and dissolution. Innovative technologies such as freeze-drying, spray drying are highlighted for their potential in creating ODTs with improved mechanical strength, stability, and controlled drug release profiles. Furthermore, the integration of nanotechnology and nanomaterials is explored, showcasing their ability to provide precise control over drug release kinetics and bioavailability enhancement. Patient-centric design principles are woven throughout the review, emphasizing the need to tailor ODT formulations to meet the specific requirements of diverse patient populations. This includes considerations for geriatric patients with reduced saliva production and pediatric patients with unique dosing needs, ensuring safe and effective medication administration. The review also touches upon environmental sustainability in pharmaceutical manufacturing by examining the emergence of eco-friendly ODT materials and production processes. The

utilization of biodegradable polymers and sustainable resources aligns with global efforts to reduce the ecological footprint of the pharmaceutical industry.

Keyword: Orodispersible, Pediatric, Regulatory Guidance, Dosage form.

INTRODUCTION

In the ever-evolving landscape of pharmaceuticals, the quest for enhanced drug delivery methods that optimize patient compliance, efficacy, and overall therapeutic outcomes remains an unceasing endeavor. Orodispersible tablets (ODTs) have emerged as a formidable innovation, offering a promising solution to the challenges posed by traditional oral medication administration. [1] These tablets, designed to disintegrate rapidly in the oral cavity without the need for water, have captured the attention of researchers, pharmaceutical companies, and healthcare professionals alike [2] The pursuit of excellence in ODT formulations has led to a dynamic exploration of novel technologies and the identification of emerging trends that are reshaping the way we approach oral drug delivery. [3] This comprehensive review, titled "Advancements in Orodispersible Tablet Formulations: A Comprehensive Review of Novel Technologies and Emerging Trends," aims to provide a comprehensive and up-to-date overview of the remarkable strides made in this field. [4] In this era of precision medicine and personalized healthcare, it is crucial to recognize that a one-size-fits-all approach to drug delivery may no longer suffice. ODTs represent a versatile platform that not only addresses the diverse needs of patients but also caters to environmental sustainability concerns. [5] The integration of cutting-edge technologies, such as nanotechnology and 3D printing, has expanded the horizons of ODT design, allowing for precise control over drug release kinetics and bioavailability enhancement. [6] Moreover, as the healthcare landscape continues to evolve, ODTs are positioned at the nexus of telehealth and patient-centric care. Their adaptability to accommodate individualized dosing regimens, coupled with their convenience and palatability, makes them a compelling choice for modern healthcare systems. This review embarks on a comprehensive journey through the realms of ODT formulation, diving deep into the formulation strategies, taste-masking techniques, eco-friendly materials, and patient-specific considerations that have emerged as pivotal factors in shaping the present and future of ODTs. Furthermore, it explores the current market dynamics and prospects, shedding light on the challenges and opportunities that lie ahead. [7] we endeavor to illuminate the path paved by advancements in ODT formulations, providing a valuable resource for researchers, pharmaceutical companies, and healthcare practitioners committed to elevating the standards of medication delivery and enhancing the patient experience. [8]

Orodispersible Tablets for Paediatric:

Pediatrics and geriatrics encompass diverse patient populations, necessitating tailored approaches for creating suitable dosage forms. Advances in pharmaceutical technology, such as Fixed-Dose Combinations (FDCs), multi-particulates, and orodispersible dosage forms, offer unique avenues for innovating and developing appropriate formulations for both established and emerging drugs. Despite the implementation of the European Union's regulation on medicinal products for pediatric use in 2007, which aimed to enhance rational,

evidence-based prescribing and age-appropriate formulations for children, many products still lack essential pediatric data. [9] In contemporary medicine, the availability of dosage forms suitable for children is essential and constitutes a fundamental requirement for effective pediatric drug treatment. Experts have long advocated for a fundamental change, moving away from traditional liquid forms towards innovative oral solid dosage forms. [10] A novel formulation approach has emerged, introducing the latest advancements in drug delivery systems in the form of orally disintegrating mini tablets (ODMTs). These ODMTs leverage the beneficial characteristics of both orally disintegrating tablets (ODTs) and mini tablets, with a specific focus on pediatric therapy. Consequently, ODMTs can be regarded as advanced, compact versions of ODTs tailored for use in pediatric patients. Mini ODTs typically range from 2 to 4 mm in diameter, accommodating different age groups and the specific active substances they contain. Experimental research has demonstrated that 2 mm tablet formulations are suitable for children aged 0.5 to 6 years, while 3 mm tablets can also be utilized for children between 2 and 8 years of age. Furthermore, these studies have highlighted that ODMTs containing dietary supplements may have a diameter of up to 4 mm. [11] Another crucial consideration is that when formulating oral tablets intended for pediatric use, it's imperative to ensure that the excipients incorporated into these formulations adhere to the regulations set forth by the International Harmonization Conference (ICH), the European Medicines Agency (EMA), and the European Food Safety Authority (EFSA). Furthermore, the processes for preparing and the quality controls, both before and after compression, of orally disintegrating mini tablets (ODMTs) closely resemble those employed in the production of orally disintegrating tablets (ODTs). [7]

Advantageous and Disadvantageous of ODT

Advantageous	Disadvantages
• Best for patient with oesophageal problems and have difficulties of deglutition tablets • High drug loading is possible. • Have acceptable taste and pleasant mouth feeling. • Leave minimum residue in the mouth after oral administration. • Guarantee a rapid onset of action when required. • Pleasant mouth-feel. • Cost effective	• Hygroscopic in nature. • Low amount of drug can be incorporated in each dose. • Some time it possesses mouth feeling • Highly fragile sometimes. • ODT requires special packaging for properly stabilization & safety of stable product. • Eating and drinking may become restricted

IDEAL PROPERTIES OF ODTs:

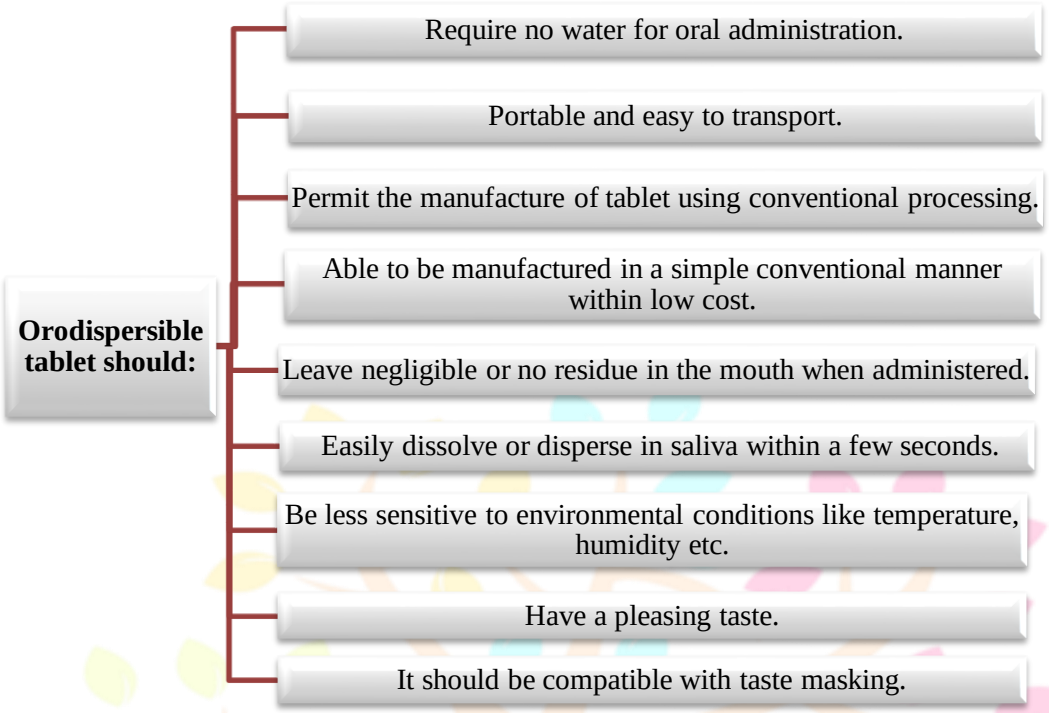


Fig. 1 Ideal properties of oral disintegrating tablets

Regulatory Guidance for Pediatric Drug Use:

Regulatory guidance concerning pediatric drug utilization embarked on its journey in 1997 under the auspices of the European Commission (EC). This initiative sought to establish new legal frameworks governing drug formulations tailored for pediatric use. [12] In 2000, the EC endorsed international discussions pertaining to clinical trials involving pediatric patients, ultimately culminating in the enforcement of the Pediatric Regulation in 2007. This regulation mandated the submission of a Pediatric Investigation Plan (PIP) to the European Medicines Agency (EMA) for evaluation by its Pediatric Committee (PDCO). It is important to note that decisions made by the EMA/PDCO regarding PIPs hold legally binding status, and drug formulation manufacturers can only proceed with marketing authorization once the EMA has validated compliance with the agreed PIP. [13]

In 2014, the EMA issued another critical guideline pertaining to the pharmaceutical development of medicines intended for pediatric use. This guideline mandated adherence to its provisions in the pharmaceutical development process for children aged from birth to 18 years. The primary objective of this regulation is to expedite the creation of pediatric drug formulations appropriate for different age groups within this range. Importantly, the Pediatric Committee (PDCO), EMA, and the Committee for Medicinal Products for Human Use (CHMP) do not seek to impose new constraints but rather strive to provide comprehensive guidance to facilitate the development of pediatric-specific drug formulations. [14] While both the U.S. Food and Drug

Administration (FDA) and EMA have been involved in pediatric drug formulation studies since 1979, it's notable that there is presently no unified guidance from the FDA on this matter.

Limitations in ODMT's

1. Orodispersible tablets (ODTs) face limitations in terms of mechanical strength, rendering them nsuitable for traditional tablet applications. ODTs are characterized by their porous and delicately molded matrix, resulting in tablets that are prone to friability and brittleness.
2. The formulation of ODTs can present challenges, particularly when dealing with bitter-tasting drugs. Consequently, the incorporation of taste-masking materials becomes imperative to enhance palatability.
3. ODT formulations exhibit hygroscopic tendencies, necessitating the use of specialized packaging materials to safeguard their physical integrity and ensure stability.
4. Reduced salivary flow can impact the bioavailability of ODT formulations, underscoring the importance of saliva in the disintegration and dissolution processes.
5. Orodispersible Mini-Tablets (ODMTs) impose limitations on drug load capacity, typically accommodating up to 6 mg per tablet [7]

Techniques for preparing ODTs.

Many techniques have been reported for the formulation of Orodispersible tablets.

- Freeze drying/lyophilization
- Tablet Moulding
- Spray drying
- Sublimation
- Direct compression
- Mass extrusion
- Wet Granulation
- Dry Granulation
- Melt Granulation
- Phase transition process
- Three-dimensional Printing (3DP)
- Cotton Candy Process
- Nanonization
- Effervescent Method
- Hot melt extrusion
- Solid dispersion extrusion
- Rolling method

CONVENTIONAL TECHNIQUES

1. Freeze Drying (Lyophilization):

Lyophilization is a specialized process designed to dehydrate heat-sensitive active ingredients at low temperatures by employing vacuum conditions to facilitate water removal through sublimation [7] Drugs prepared using lyophilization exhibit rapid disintegration in the oral cavity due to the swift penetration of saliva into the porous structure.

The freeze-drying process typically involves three key phases:

- ❖ Freezing the material to reduce it below the eutectic point.
- ❖ Primary drying to bring down the moisture content to approximately 4% w/w of the dry product.
- ❖ Secondary drying to further reduce the bound moisture to the desired final volume.

Advantages of this method include faster dissolution compared to other solid products. However, lyophilization is associated with drawbacks such as high equipment costs and reduced physical durability when packaged in blister packs [15] Lyophilization is a technique employed to dissolve or disperse active drugs within an aqueous carrier/polymer solution. This mixture is poured into preformed blister packs, frozen, and subsequently freeze-dried. An aluminum foil backing is then applied using a blister-sealing machine, and the sealed blisters are packaged for distribution. Major disadvantages of lyophilization encompass its costliness, time-consuming nature, fragility, and susceptibility to stability issues

2. Tablet Molding:

This method is employed to create tablets characterized by solid dispersions with enhanced taste profiles, often achieved through the incorporation of water-soluble sugars. The tablet molding process encompasses two primary techniques: solvent-based and heat-based molding. In the solvent method, the powder blend is moistened with a hydroalcoholic solvent, while the heat method involves the application of low-pressure compression within molded plates to form a wetted mass. Tablets produced through these methods tend to be less compact than conventionally compressed tablets, offering a porous structure that accelerates dissolution. Heat molding, for instance, involves the preparation of a mixture containing the drug, agar, and sugar in a suspension. This mixture is then poured into blister packaging wells, allowed to solidify at room temperature, and subsequently dried under vacuum conditions at 30°C. The advantages of tablet molding include the creation of a dispersive matrix that promotes rapid disintegration and enhances taste. However, it's worth noting that tablets produced via this method may be susceptible to erosion and breakage during handling and when opening blister packages.

3. Spray Drying:

In this method, a particulate support matrix is employed to create a highly porous and finely powdered substance, which is subsequently blended with active ingredients and compressed to form tablets. Various components, such as hydrolyzed and non-hydrolyzed gelatins, mannitol, sodium starch glycolate, or crosscarmellose sodium, along with acidic and alkaline materials, are used to enhance the disintegration and

dissolution properties of tablets crafted from spray-dried powder. Remarkably, tablets prepared using this technique disintegrate in an aqueous medium within a mere 20 seconds.The notable advantages of this approach include the swift disintegration of tablets, as observed in studies [16] However, it's important to acknowledge certain drawbacks, including the relatively high production cost and the inherent fragility of the resulting tablets. Tablets created through this method exhibit substantial porosity, which, while contributing to their rapid disintegration, renders them unsuitable for conventional packaging methods, as noted in research [7]

4. Direct compression:

Direct compression stands out as the most cost-effective tablet manufacturing method, largely owing to advancements in excipient technology. This technique benefits from the availability of tabulating excipients with improved flow, compressibility, and disintegration properties. These excipients, which include tablet disintegrants, effervescent agents, and sugar-based components, enable the fabrication of tablets using conventional manufacturing and packaging machinery. For instance, Flash tab, a notable product, incorporates coated drug crystals and microgranules alongside disintegrants. Sugar-based excipients, classified by Mizumoto et al. into two types based on their moldability and dissolution rate, offer further versatility. Type I saccharides exhibit high dissolution rates but low moldability (e.g., lactose and mannitol), while Type II saccharides possess high moldability but lower dissolution rates (e.g., maltose and maltitol) [17]

Mechanism of Action of Superdisitegrats:

The tablet breaks to primary particles by one or more of the mechanisms listed below

1. Porosity and capillary action (Wicking)
2. Swelling
3. Due to deformation
4. Because of heat of wetting (air expansion)
5. Due to disintegrating particle/particle repulsive forces
6. Due to release of gases
7. By Enzymatic Reaction

PATENTED TECHNOLOGIE:

Pharmaceutical firms have pioneered technologies and methodologies rooted in formulation principles. Orally Disintegrating Tablets (ODTs) exhibit swift dissolution owing to the rapid ingress of water into the tablet matrix, leading to rapid disintegration.

Different Patented Technologies:

1) Zydis Technology:

Zydis represents a distinctive freeze-dried tablet formulation wherein the drug is either physically encapsulated or dissolved within a matrix of rapidly dissolving carrier materials. This formulation comprises polymers like gelatin, dextran, or alginates, as well as saccharides such as mannitol or sorbitol. The manufacturing process involves lyophilizing the drug within a matrix composed of water-soluble carriers, such as gelatin. Currently, over twenty products leverage Zydis technology, including well-known ones like Claritin Reditab, Dimetapp Quick Dissolve, Feldene Melt, Maxalt-MLT, Pepcid RPD, Zofran ODT, and Zyprexa Zydis.

2) Orasolv Technology:

OraSolv represents Cima's pioneering fast-dissolving/disintegrating dosage form, which blends taste-masked drug components with an effervescent excipient system. Importantly, it can be manufactured using standard processes and equipment. This technology is utilized in eight available products, including Triaminic Soft chew formulations, Tempra FirsTabs, and Remeron SolTab. [18]

3)Durasolv Technology:

DuraSolv stands as the patented technology developed by CIMA labs. Tablets produced using this technology are composed of drug, filler, and a lubricant. These tablets are crafted using conventional tablet manufacturing equipment and exhibit strong structural integrity. [19]

DuraSolv represents Cima's second-generation technology for mouth-dissolving/disintegrating formulations, incorporated within a matrix that includes non-direct compression filler, lubricant, and wicking agent. These components are compressed into tablet form. DuraSolv is particularly well-suited for products with lower quantities of active ingredients.

4) Wowtab Technology:

The WOWTAB symbolizes a tablet designed for consumption without the need for water, as noted by PB Patil. Wowtab, a fast-dissolving/disintegrating tablet, has been a staple in the Japanese market for several years. The Wowtab technology relies on sugar and sugar-like excipients to achieve effective taste masking and provide a pleasant mouthfeel. Mizumoto et al. have categorized sugar-based excipients into two distinct types based on their characteristics in terms of moldability and dissolution rate.

Type I Saccharides, such as lactose and mannitol, exhibit low moldability but a high dissolution rate. On the other hand, Type II Saccharides, like maltose and maltitol, possess high moldability but a slower dissolution rate. By combining these two saccharides, a tablet formulation with both high hardness and rapid dissolution rate is created. Wowtab products dissolve in 15 seconds or less, as described by Jaybhaye Aarti.

5) Flashdose Technology:

The Flash Dose technology, patented by Fuisz Technologies Ltd., is behind the innovation of Nurofen Meltlet – a novel form of ibuprofen tablets that dissolve in the mouth, introduced by Biovail Corporation, as highlighted by R. Santosh Kumar et al. [20]

In the Flash Dose process, a spinning mechanism is employed to create a floss-like crystalline structure, which can then be compressed into tablet form. Fuisz Technologies has also developed the patented Shearform method. Shearform utilizes small saccharide spheres to effectively carry the drug. Additionally, Ceform presents an alternative approach using microspheres for taste masking, as described by Jaybhaye Aarti.

6) Flash Tab Technology:

This technology presents an innovative approach to the creation of oro-dispersible tablets, as noted by Mukesh Chandra Sharma et al.The Flashtab technology, patented by Prographarm Laboratories according to Patil AV et al, is responsible for producing tablets with accelerated disintegration rates in the mouth. This rapid disintegration is attributed to the presence of active substances in the form of either coated microcrystals or uncoated microgranules. [21]

Coated multiparticles containing active ingredients can be prepared using conventional methods, as mentioned by Mukesh Chandra Sharma in 2022. The resulting tablets from this process possess characteristics such as softness, brittleness, sensitivity to humidity, and rapid dissolution, as pointed out by Jassem NA. [22]

7) Quicksolv Technology:

Janssen Pharmaceuticals has secured a patent for their QuickSolv technology, an innovative approach that utilizes two solvents to create a matrix with instant disintegration properties. The methodology involves dissolving the components of the matrix in water, freezing the mixture, and subsequently eliminating the water by employing an excess of alcohol. The resulting product exhibits consistent porosity and sufficient structural integrity for easy handling.

8) Lyoc Technology:

The Lyoc technology, patented by Pharmalyoc, encompasses a process where an oil-in-water emulsion is introduced into blister cavities, followed by a freeze-drying step. To prevent non-uniformity, an inert filler is incorporated to enhance viscosity and mitigate sedimentation. However, it's important to note that a higher proportion of filler can decrease tablet porosity, potentially leading to slower disintegration.

9) Ziplets Technology:

Eurand, based in Pessano con Bornago, Italy, introduced Ziplets technology, which is applicable to water-insoluble compounds, serving as both bulk actives and as coated micro-particles. However, tablets primarily comprising water-soluble components may have a tendency to dissolve instead of disintegrate. This can lead

to prolonged disintegration times due to the formation of concentrated and viscous solutions, as highlighted by Jaybhaye Aarti.

With Ziplets technology, drug particles can be conveniently packed into push-through blisters or bottles, eliminating the necessity for specialized packaging, as pointed out by 16 Arora P. et al. [23]

Conventional Drug Delivery Systems for Pediatric Usage: -

Conventional solid dosage forms and liquid drug formulations restrict the delivery of drugs to pediatric patients.

Liquid dosage forms:

Because young children often struggle with swallowing and may face challenges with the size of medications, liquid formulations are typically the preferred option. Nonetheless, there are drawbacks, including the need for frequent dosing and the difficulty in masking bitter tastes. Innovative drug delivery systems like ODTs (Orally Disintegrating Tablets) or mini tablets are potential solutions to address these issues.

Solid dosage forms:

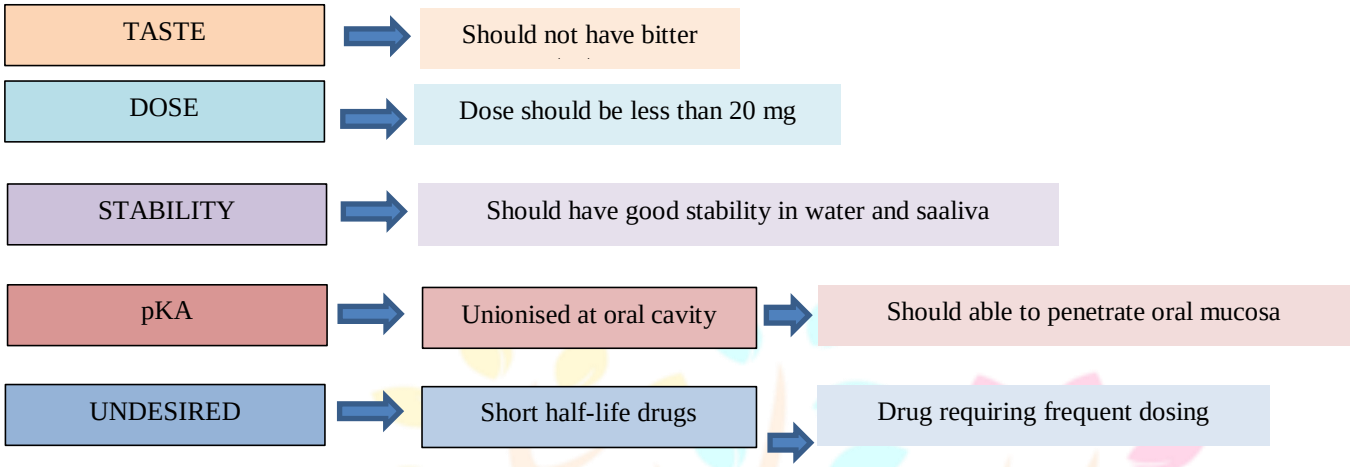
Solid dosage forms are frequently favored due to their cost-effectiveness, extended shelf life, and effectiveness in masking bitter tastes. Nonetheless, traditional solid dosage forms lack the flexibility to adjust doses easily. To address this limitation, an application device known as the 'solid dosage pen' has been created to provide dose flexibility. This pen enables users to cut tablets to their preferred length, allowing for customized dosing. However, concerns persist regarding the practicality and safety of this approach. In recent years, Orally Disintegrating Mini Tablets (ODMTs) that can be administered to very young children have gained popularity as an alternative solution.

Novel oral drug delivery systems for pediatric usage:

Mini tablets and ODTs offer more convenient dosing flexibility and do not pose swallowing difficulties when used in pediatric applications. Research has demonstrated that even infants as young as one month old can more readily accept and utilize 2mm diameter tablets compared to syrups, enhancing both dose flexibility and ease of administration. Mini tablets can be employed to achieve either immediate or modified release in pediatric drug formulations. A novel approach has been devised to adapt orally disintegrating tablets, making them well-suited for pediatric use. [24]

Factors To Be Considered for the Selection of the Drug: -

Factors such as taste, dose, stability, and pKA should be taken into account when selecting a drug. Are follow:



Excipients Used in Oral Disintegrating Tablets:

Table 1: Excipients Used in Oral Disintegrating Tablets

Sr. No.	Types Of Excipients	Examples	Function	W/W %
1.	Binders	Polyvinylpyrolidone (PVP), polyvinyl alcohol (PVA), hydroxypropyl methylcellulose (HPMC), etc.	Maintains integrity of dosage form prior to administration	5-10 %
2.	Super disintegrating agents	Sodium starch glycolate (SSG), crospovidone, croscarmellose sodium, Polacrilin potassium, modified corn starch, carboxy methylcellulose (CMC), microcrystalline cellulose (MCC), Pregelatinzed starch etc.	The presence of other formulation ingredients such as water-soluble excipients and effervescent agents increases the rate of disintegration, making it necessary to use a super disintegrant for fast dissolving tablets.	1-15 %
3.	Diluents	Magnesium trisilicate, calcium sulfate, magnesium carbonate, etc.	Increase weight and content uniformity of formulation.	0-85 %
4.	Taste masking agents	Sorbitol, mannitol, xylitol, dextrose, fructose, etc.	Hide the bitter or unpleasant taste of drug.	0-10 %

5.	Antistatic agents	Polyoxyethylene stearates, polyoxyethylene sorbitane fatty acid esters, sodium dodecyl sulfate, sodium lauryle sulfate (SLS), etc.	Used as surfactant	0-10 %
6.	Flavors	Peppermint flavor, cooling flavor, flavor oils and flavoring aromatic oil, peppermint oil, clove oil, bay oil, anise oil, eucalyptus oil thyme oil, oil of bitter almonds. Flavoring agents include, vanilla, citrus oils, fruit essences.	Increases Patient compliance and acceptability	0-5%
7.	Sweeteners and sugar based excipients	Artificial sweeteners like Aspartame, Sugars derivatives. Bulking agents like dextrose, fructose, isomalt, lactilol, maltitol, maltose, mannitol, sorbitol, starch hydrolysate, polydextrose and xylitol.	Sugar based excipients act as bulking agents, imparting taste masking and a pleasing mouth feel.	1-5%%
8.	Surface Active agents	Sodiumdoecylsulfate, sodiumlaurylsulfate, polyoxyethylene sorbitan fatty acid esters (Tweens), sorbitan fatty acid esters (Spans), polyoxyethylene stearates.	Reducing interfacial tension enhances solubilization of FDT.	0-5%
9.	Color	Sunset yellow, Amaranth, Red iron oxide	Dosing form enhances appearance and organoleptic properties.	0-5%
10.	Lubricants	Stearic acid, Magnesium stearates, Zinc state, calcium state, talc, polyethylene glycol, liquid paraffin, magnesium lauryl sulfate, colloidal silicon dioxide	Lubricant is used to reduce friction and wear by introducing a lubricating film between mechanical moving parts of a tablet punching machine.	0-5%

11.	Fillers	Directly compressible spray dried Mannitol, Sorbitol, xylitol, calcium carbonate, magnesium carbonate, calcium phosphate, calcium sulfate, pregelatinzed starch, magnesium trisilicate, aluminium hydroxide	Enhances bulk of dosage form	0-5%

In vitro disintegration method for ODT: -

Table 2: In Vitro Disintegration Method

Method	Feature	Parameter	Action	Reference
Pharmacopoeial	Six tablets were placed into the tubes of the disintegration apparatus and the test was started. The disintegration time was measured semi-automatically.	Medium 900ml, temp. 37°C	–Water wicking –Mechanical destructive force caused by the movement of the basket.	[25]
Pharmacopoeial – modified	Instead of one plastic disk, every tablet was covered with five of them, and only one tablet was tested during one trial.	Medium 900ml, Temp. 37°C	–Water wicking –Pressure acting on the tablet by the five plastic disks weight.	[26]
Modified USP Apparatus II (Paddle Method)	One litre cylindrical vessel, paddle as stirring element, basket sinker with ODT was placed in middle of vessel and hang by a hook to the lead of vessel with distance of 6-8.5 cm	Medium 900ml, Temp. 37°C, Paddle, 100 rpm.	–Water wicking, –Rotating paddle causes water stirring leading to the tablet erosion.	[27]

Rotating shaft method	Tablet was placed on a wire gauze, slightly immersed in water, and pressed by the rotary shaft toward the gauze. Then it was grinded by the rotary motion of the shaft until it disintegrated completely	Medium 450ml, Temp. 37°C	–Water wicking –Tablet grinding between rotating shaft and metal plate. –Pressure caused by the load of a rotating shaft acting on the tablet	[28]
Test-tube method	The tablet was placed into the test-tube with 2 ml of distilled water, and its disintegration time was measured with a stopwatch.	Medium 2ml, Temp. Ambient	–Water wicking	[29]
Sieve method	Two different sieve methods were used. the tablet was placed on the stainless steel sieve (2 mm aperture), and distilled water was dropped on its upper surface with constant speed of 4 mL/min.	4 ml/min., temp. Ambient	Water wicking	[30]
Sieve method with shaker	A glass tube with a sieve on its bottom was used. It was immersed in distilled water about 1 mm deep. The tablet was dropped on the sieve, and the time measurement was started. The tube was constantly shaken with a reciprocating bath shaker (150 rpm).	Medium 3 ml, temp. 37°C	–Water wicking, –Water agitation caused by reciprocating shaker.	[31]

Own construction apparatus (BJKSN-13 apparatus)	The motion of the shaft was different, and the registration mechanism was based on a magnetic sensor instead of an electric circuit. Real time changes in tablet thickness during disintegration were measured and recorded by computer software.	Medium 5 ml, temp. 37°C	–Water wicking –Tablet grinding between rotating shaft and metal plate. –Pressure caused by the load of a rotating shaft acting on the tablet	[32,33]
Wetting test	6 tablets of each formulation. A tablet weighed prior to the test was placed in a petri dish with a red dye solution, and the time of wetting the whole surface of the tablet was measured.	Medium 7 ml, temp. Ambient	–Water wicking	[34]
Pharmatest PTZ Auto	Only one ODT at a time was placed into the disintegration apparatus and the time taken (seconds) for the tablet to fully disintegrate was recorded.	Temp. 37 °C ± 2°C, Medium 6.8 buffer	–Water wicking	[35]
USP disintegration test apparatus	6 glass tubes which are 3 inches long, open at the top, held against a 10 mesh screen, at the bottom end of the basket rack assembly	Medium 1000ml Temp. 37 °C ± 2°C.	–Water wicking –Pressure acting on the tablet by the plastic disks weight.	[36]

Packaging Considerations:

Packaging plays a pivotal role in the development of Orodispersible Tablets (ODTs) since the excipients employed must swiftly disintegrate or dissolve with minimal water and be resistant to moisture absorption. Diverse techniques yield ODTs with varying mechanical strengths. Notably, Zydis-designed ODTs exhibit

porosity, rendering them less physically resistant and less prone to moisture-induced degradation [37] Lyophilized products necessitate specialized packaging, including options like Zydis, Lyoc, Quicksolv, and Nanocrystal, all characterized by their porous nature and reduced vulnerability to moisture. However, it's worth noting that these materials may pose challenges in high humidity conditions [38] For rapidly dispersing or dissolving oral delivery routes, such as single pouches, blister cards, multiple unit dispensers, and continuous roll dispensers, careful attention must be paid to packaging requirements. Each of these options presents unique advantages and considerations in ensuring the efficacy and stability of ODTs [39]

Future Prospects:

Conventional tablets are inadequate for delivering drugs like protein and peptide-based therapeutics due to their limited bioavailability and rapid degradation in the stomach. Injections, while effective, may not always be the preferred method for administering these substances. [40] Inhalation is a viable approach for drug delivery, but most research in the biopharmaceutical field has focused on low molecular weight compounds. However, there is growing interest in exploring oral delivery options for high molecular weight proteins and peptides, and Orodispersible Tablets (ODTs) offer a promising solution. ODTs can release these drugs in the oral cavity, providing a compelling alternative for delivering these complex and valuable biopharmaceuticals. [41]

CONCLUSION

In conclusion, Orodispersible Tablets (ODTs) and Orodispersible Mini-Tablets (ODMTs) represent a promising paradigm shift in pharmaceutical therapy, with a particular emphasis on enhancing pediatric medication administration. These novel dosage forms offer distinct advantages over traditional oral medications, including heightened patient compliance, convenience, rapid onset of action, and improved bioavailability. ODTs, renowned for their versatility, cater to a wide age group, while ODMTs combine the advantages of both liquid and solid forms, providing ease of use, dose flexibility, and an acceptable taste profile. The pharmaceutical industry's growing adoption of ODTs reflects the recognition of the challenges posed by swallowing conventional tablets and capsules, which often result in noncompliance and hinder therapeutic efficacy. ODTs and ODMTs provide a patient-centric solution that addresses these concerns and contributes to improved medication adherence. Furthermore, ODMTs hold considerable promise in pharmaceutical manufacturing due to their compact size, ease of administration, and the availability of diverse preparation technologies. These attributes make them an attractive choice for pharmaceutical companies seeking to develop efficient and patient-focused drug delivery systems. As we advance, it is imperative to refine methods for measuring ODT disintegration time, accounting for variables such as tablet volume, temperature, and the forces applied during testing. Striking a balance between disintegration time and mechanical strength remains crucial. High-porosity tablets disintegrate rapidly but may exhibit lower mechanical strength, while low-porosity tablets offer greater mechanical strength alongside rapid disintegration.

ACKNOWLEDGEMENT

The authors are very thankful to the management of Smt. Kishoritai Bhoyar college of Pharmacy, Kamptee, Nagpur, for providing necessary facilities and encouragement.

DECLARATION OF INTEREST

The authors declare no conflict of interest, financial or otherwise.

REFERENCES

1. Rao NR, Shravani B, Reddy MS. Overview on buccal drug delivery systems. Journal of pharmaceutical sciences and research. 2013 Apr 1;5(4):80.
2. Ramjiyani KM, Jethara SI, Patel MR. Fast dissolving tablets: novel approach to drug delivery. World Journal of Pharmaceutical Research. 2015;4(3):1197-215.
3. Dey P, Maiti S. Orodispersible tablets: A new trend in drug delivery. Journal of natural science, biology, and medicine. 2010 Jul;1(1):2.
4. Singh K, Saroha K, Mohan R, Kumar A, Pandit C. Orodispersible tablets: Development, technologies and evaluation: An overview. The pharma Research.;8(1):128-47.
5. Gupta MS, Kumar TP, Gowda DV, Rosenholm JM. Orodispersible films: Conception to quality by design. Advanced Drug Delivery Reviews. 2021 Nov 1;178:113983.
6. Cilurzo F, Musazzi UM, Franzé S, Selmin F, Minghetti P. Orodispersible dosage forms: Biopharmaceutical improvements and regulatory requirements. Drug discovery today. 2018 Feb 1;23(2):251-9.
7. Comoglu T, Dilek Ozyilmaz E. Orally disintegrating tablets and orally disintegrating mini tablets–novel dosage forms for pediatric use. Pharmaceutical Development and technology. 2019 Aug 9;24(7):902-14.
8. Preis, Maren, Miriam Pein, and Jörg Breitkreutz. "Development of a taste-masked orodispersible film containing dimenhydrinate." *Pharmaceutics* 4, no. 4 (2012): 551-562.
9. Hanning SM, Lopez FL, Wong IC, Ernest TB, Tuleu C, Gul MO. Patient centric formulations for paediatrics and geriatrics: Similarities and differences. International Journal of Pharmaceutics. 2016 Oct 30;512(2):355-9.
10. Wiedey R, Kokott M, Breitkreutz J. Orodispersible tablets for pediatric drug delivery: Current challenges and recent advances. Expert Opinion on Drug Delivery. 2021 Dec 2;18(12):1873-90.
11. Lopez FL, Ernest TB, Tuleu C, Gul MO. Formulation approaches to pediatric oral drug delivery: benefits and limitations of current platforms. Expert opinion on drug delivery. 2015 Nov 2;12(11):1727-40.
12. Preis, Maren, Miriam Pein, and Jörg Breitkreutz. "Development of a taste-masked orodispersible film containing dimenhydrinate." *Pharmaceutics* 4, no. 4 (2012): 551-562.

13. Sotoyama M, Uchida S, Tanaka S, Hakamata A, Odagiri K, Inui N, Watanabe H, Namiki N. Citric acid suppresses the bitter taste of olopatadine hydrochloride orally disintegrating tablets. Biological and Pharmaceutical Bulletin. 2017 Apr 1;40(4):451-7.
14. Davis PJ, Fertal KM, Boretsky KR, Fedel GM, Ingram MD, Woelfel SK, Hoffmann PC, Gurnaney H, Young MC. The effects of oral ondansetron disintegrating tablets for prevention of at-home emesis in pediatric patients after ear-nose-throat surgery. Anesthesia & Analgesia. 2008 Apr 1;106(4):1117-21.
15. Ascher-Svanum H, Furiak NM, Lawson AH, Klein TM, Smolen LJ, Conley RR, Culler SD. Cost-effectiveness of several atypical antipsychotics in orally disintegrating tablets compared with standard oral tablets in the treatment of schizophrenia in the United States. Journal of Medical Economics. 2012 Jan 1;15(3):531-47.
16. Arora P, Sethi VA. Orodispersible tablets: A comprehensive review. Int J Res Dev Pharm Life Sci. 2013 Feb;2(2):270-84.
17. Rewar S, Singh CJ, Bansal BK, Pareek R, Sharma AK. Oral dispersible tablets: An overview; development, technologies and evaluation. International Journal of Research and Development in Pharmacy & Life Sciences. 2014 Nov 15;3(6):1245-57.
18. Patil PB, More VN, Tour NS. Recent trends in orodispersible tablets–An overview of formulation technology and future prospects. International Journal of Pharma Sciences and Research. 2015;6(7):1056-66.
19. Jassem NA. Orodispersible Tablets: A Review on Recent Trends in Drug Delivery. Journal of Drug Delivery Technology. 2022;12(1):432-6.
20. Orodispersible drug formulations for children and elderly Marta Slavkova, Jorg Breitkreutz 2015. Slavkova, Marta, and Jörg Breitkreutz. "Orodispersible drug formulations for children and elderly." *European Journal of Pharmaceutical Sciences* 75 (2015): 2-9.
21. Gupta, Maram Suresh, Tegginamath Pramod Kumar, Devegowda Vishkante Gowda, and Jessica M. Rosenholm. "Orodispersible films: Conception to quality by design." *Advanced Drug Delivery Reviews* 178 (2021): 113983.
22. Gupta DK, Maurya A, Varshney MM. Orodispersible tablets: An overview of formulation and technology. World Journal of Pharmacy and Pharmaceutical Sciences. 2020 Aug 13;9(10):1406-18.
23. Khan WR, Kumar V, Mehetre J, Chaurey M. Fast Dispersing Tablets (FDT) Based Technology: A Review at a Glance.
24. Ghourichay MP, Kiaie SH, Nokhodchi A, Javadzadeh Y. Formulation and Quality Control of Orally Disintegrating Tablets (ODTs): Recent Advances and Perspectives. BioMed Research International. 2021 Dec 24;2021.
25. Aarti J, Sonali J, Ganesh D. Orodispersible tablets: A comprehensive review. Research Journal of Pharmacy and Technology. 2014 Mar 1;7(3):8.
26. Sharma MC, Leel M. A Review: Oral Dispersible Tablets. Int J Drug Dev & Res. 2022;14(1).

27. Kumar RS, Ghosh A. FAST DISSOLVING TABLETS: PATIENT COMPLIANCE DOSAGE FORMS.
28. Ganesh NS, Deshpande KB. Orodispersible tablets: An overview of formulation and technology. International Journal of Pharma and Bio Sciences. 2011;2(1):726-34.
29. Patil AV, Sali DH, Reddi SS, Wargade NS, Mohaptra SK, Paygude BV. Recent trends and formulation technology of orodispersible tablets. Journal of Pharmacy Research. 2011 Mar;4(3):924-8.
30. Thabet Y, Slavkova M, Breitkreutz J. 10 years EU regulation of pediatric medicines–impact on cardiovascular drug formulations. Expert Opinion on Drug Delivery. 2018 Mar 4;15(3):261-70.
31. Bandari S, Mittapalli RK, Gannu R. Orodispersible tablets: An overview. Asian Journal of Pharmaceutics (AJP). 2008;2(1).
32. Shravani B, Rao NR, Pragna G, Reddy MS. FORMULATION AND EVALUATION OF ORAL DISINTEGRATING TABLETS OF MONTELUKAST SODIUM: EFFECT OF FUNCTIONALITY OF SUPERDISINTEGRANTS.
33. Heer D, Aggarwal G, Kumar SH. Recent trends of fast dissolving drug delivery system–an overview of formulation technology. Pharmacophore. 2013 Jan 1;4(1):1-9.
34. Madhumathi I, Hemalatha B, Padmalatha K. Fast Dissolving Tablets: A Review. Asian Journal of Pharmacy and Technology. 2022 May 25;12(2):183-9.
35. Pawar YN, Gangurde AB, Patil ND. PHARMACEUTICAL SCIENCES.
36. Wadher K, Dhote K, Mane M, Khapne A, Milind AG. Orodispersible Dosage Form: Advancement and Challenges. Int J Pharma Res Health Sci. 2019;7(4):3013-9.
37. Sheshala R, Khan N, Chitneni M, Darwis Y. Formulation and in vivo evaluation of ondansetron orally disintegrating tablets using different superdisintegrants. Archives of pharmacal research. 2011 Nov;34(11):1945-56.
38. Abd Elbary A, Ali AA, Aboud HM. Enhanced dissolution of meloxicam from orodispersible tablets prepared by different methods. Bulletin of Faculty of Pharmacy, Cairo University. 2012 Dec 1;50(2):89-97.
39. Brniak W, Jachowicz R, Pelka P. The practical approach to the evaluation of methods used to determine the disintegration time of orally disintegrating tablets (ODTs). Saudi Pharmaceutical Journal. 2015 Sep 1;23(4):437-43.
40. Pabari RM, Ramtoola Z. Effect of a disintegration mechanism on wetting, water absorption, and disintegration time of orodispersible tablets. Journal of young pharmacists. 2012 Jul 1;4(3):157-63.
41. Mahesh E, Kumar GK, Ahmed MG, Kumar PK. Formulation and evaluation of montelukast sodium fast dissolving tablets. Asian J Biomed Pharm Sci. 2012 Dec 15;2:75-82.