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REVIEW ARTICLE

Oral Dispersible Tablets -Mechanisms, Formulation and Evaluation

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ABSTRACT
Pharmaceutical scientists are learning more about the physicochemical and biological factors that affect drug delivery systems' efficacy, which leads to an advancement in their sophistication. Due to improved patient compliance, orally disintegrating tablets (ODTs) have drawn a lot of attention in the last thirty years as a preferable substitute for traditional tablets and capsules. When placed on the tongue, ODTs—solid dosage forms containing medication—disintegrate quickly, often within a few seconds. The 1980s saw the introduction of ODT technologies' products to the market, which have since seen a steady increase in demand and a quick expansion of their product pipelines. New ODT technologies cover a wide range of medicinal drugs and sufferer demands, from improved life-process administration to easy-to-use dosage for patients with dysphagia in the psychiatric, paediatric, and elderly populations. This has prompted researchers and businesses to develop fresh methods of technology and oral disintegration in this area. This article's goal is to cover the evolution of ODTs, desired qualities, product assessment, formulation difficulties, the active components and excipients used in the formation of ODTs, address the advantages and disadvantages of various ODT formulation and preparation procedures, and provide solutions for ODT-related issues.
Keywords: *Orally disintegrating tablet, Dysphagia, Psychiatric, Paediatric.*

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INTRODUCTION

Because of its simplicity of consumption, potentiality to prevent pain, flexibility (to accept different types of drug candidates), and—above all—sufferer compliance, oral administration is the broadly used method.Since solid oral delivery devices don't require sterile conditions, their production costs are lower. Many different types of pharmaceutical research are being done to create novel dosage formulations that can be taken orally. Most of these initiatives have been directed toward improving patient compliance or developing innovative drug delivery methods(1). Product development scientists have found that oral disintegrating systems are the most preferred dose forms among those created to make medicine administration easier.Like this, patients find the oral cavity to be very pleasant; the mucosa is richly blood-supplied, reasonably permeable, and Almost devoid of Langerhans cells, allowing the mucosa to be resistant to potential allergens(2).Pharmaceutical technologists have created Orally Disintegrating Tablets (ODTs), a unique oral dose form that dissolves quickly in saliva and doesn't require watering down to meet these medicinal needs. medication absorption and dissolution, clinical effect onset, and medication bioavailability may all be markedly higher than with traditional dose forms(3). Chewable pills are not the same as the new ODTs, despite being on the market for a while. Patients who have trouble or pain when chewing can easily take these innovative tablets. According to recent market research, over 50% of patients choose ODTs over other dose forms10. The majority of customers would either buy ODTs or ask their doctors for them (70%), or they would prefer ODTs over ordinary pills or liquids (>80%)(4). According to the "Orange Book," an ODT is defined as "a solid dosage form containing medicinal substances, which disintegrates rapidly, usually within a matter of seconds, when placed upon the

tongue" by the US Food and Drug Administration's Centre for Drug Evaluation and Research (CDER). The European Pharmacopoeia adopted the term "Oro dispersible Tablet" to designate these dosage forms, emphasizing their relevance. The term describes a pill that dissolves quickly in the mouth before being swallowed(5). ODT medications have been created for a range of purposes, including mental illness (where patient compliance is critical for treating chronic indications like depression and schizophrenia) and migraines, for which a rapid beginning of action is vital(6).

Description of Dosage Forms for Oral Disintegration:

Lozenges, buccal tablets, and conventional sublingual tablets—all of which require more than a minute to dissolve in the mouth—should not be mistaken for ODTs. In the literature, ODTs are also known as dispersed, mouth-dissolving, quick-dissolving, fast-melting, and freeze-dried wafers.(7). An easily dissolved, thin matrix containing a medicine that may be consumed without water is called a freeze-dried wafer. To maintain physical stability, unit-dose packaging is necessary for this delicate dosage form. The medication is released when the wafer instantly dissolves in the mouth and spreads throughout the saliva. The medication is absorbed through the gastrointestinal system once the saliva is swallowed (GIT)(8). A quick-dissolving tablet is a type of oral medication that dissolves in the mouth fast and doesn't require water. The terms mouth-dissolving, rapid melting, rapid dissolving, fast-dissolving multi-particulate, and Oro dispersion tablets are also used to describe it. Within 60 seconds, the tablet dissolves in the mouth(9). The GIT and oral mucous membranes allow the active substances to be absorbed and enter the bloodstream. Some pregastric drug absorption may pass through the stomach's acids and enzymes without going through the digestive tract. The tablets can be packed in multidose containers and are generally strong in terms of physical construction(10).

Ideal properties of ODTs(3):

To set them apart from standard dose forms, ODTs had to exhibit a few ideal features. Among these dosage formulations' key desirable attributes are. There is no need for water before swallowing, but it may disintegrate in the mouth in a few seconds.

1. Provide a satisfying oral sensation.
2. Adhere to methods of disguising flavour.
3. Be lightweight and resistant to brittleness.
4. Leave very little to no residue in the oral cavity following oral administration.
5. Show minimal susceptibility to changes in temperature and humidity in the surroundings.
6. Permit heavy drug loading.
7. Flexible and easily compatible with standard processing and packaging machinery at the lowest price.

Advantages:

1. ODT created new commercial opportunities in the areas of life cycle management, patent extension, product diversification, and product promotion.
2. Ideal for travel in areas without access to water(11).
3. Push-through blisters can be packaged without the need for special packaging.
4. Standard manufacturing apparatus.
5. Economical in price.
6. Similar to traditional oral solid dose forms, it has good chemical stability.
7. Novel commercial opportunities such as lifestyle management, patent extension, product differentiation, and product promotion(12).
8. Permit heavy drug loading.
9. Offers quick medication administration through dose forms.
10. Offer the benefit of a solid preparation for a liquid drug.
11. Quick drug treatment intervention.
12. No need to chew.

Disadvantages(8):

1. ODT must be stored in a dry environment due to its hygroscopic nature.
2. It occasionally has a mouth sensation.
3. It also demonstrates the quality of effervescent, fragile granules.
4. ODT needs specialized packaging to stabilize a stable product correctly and safely.

Patient factors: Especially suitable for patients who find it difficult to consume regular tablets and capsules with an 8-ounce glass of water, are oral disintegrating dose forms. Among them are the following:

1. Individuals with difficulty chewing or swallowing solid dosage forms, regardless of age.
2. Individuals who refuse to take solid food supplements because they worry about choking.
3. Elderly folks who might not be able to take an antidepressant on a regular basis(7).

4. Eight-year-old allergic child requests a more convenient dosing type of antihistamine syrup(3).
5. A middle-aged lady with breast cancer who is receiving radiation treatment could feel too sick to take her H2-blocker.
6. A patient with schizophrenia who was institutionalized and tried to conceal a conventional tablet beneath his tongue in order to avoid taking an atypical antipsychotic tablet on a daily basis.
7. A patient who is experiencing chronic nausea, may be on the road, or has limited or no access to water(13).

ODTs-mechanism(1):

1. To attain the intended quick dissolving properties, ODTs use the following methods.
2. For the tablet to dissolve and disintegrate swiftly, water must get into the matrix of the tablet immediately.
2. Adding highly water-soluble excipients or the proper disintegrating agent to the tablet formulation.
3.A few previously unstated mechanisms cause the tablet to break down into tiny particles, which results in a drug dispersion or solution.

The three mechanisms are:

1. chemical reaction.
2. capillary action.
3. high disintegration swellability.

The elements of ODTs formulation:

Essential components in ODT formulations should enable the drug to release quickly, leading to a faster rate of dissolution. This covers the excipients (additives) as well as the pharmacologically active substances (drugs)(14).

Choosing a drug candidate: Several criteria may be considered when choosing a good medication candidate to use in the production of tablets that dissolve in the mouth. For oral disintegration and pre-gastric absorption from rapidly dissolving tablets, the following characteristics are ideal(15).

1. Without a bitter flavor.
2. A dosage less than 20 mg.
3. A molecular weight of small to moderate.
4. Good saliva and water solubility.
5. Partially combined at the oral cavity's pH.
6. Capacity to divide and diffuse into the upper GIT epithelium (log >1, or ideally >2)
7. Capacity to enter the mucosal tissue of the mouth. If the material is utilized as an active ingredient in pharmaceuticals, there are no specific restrictions. Researchers have created ODT for a range of drug classes utilized in therapy, where a rapid peak plasma concentration is required to elicit the desired pharmacological response. These include anti-allergic, anti-epileptic, anxiolytic, anti-parkinsonian, antibacterial, hypnotics, diuretics, neuroleptics, cardiovascular agents, analgesics, and erectile dysfunction drugs(3).

On the other hand, the following qualities can make them inappropriate for oral disintegration tablet delivery:

1. Frequent dosage and brief half-life.
2. Extremely bitter or unsatisfactory taste due to an inability to effectively disguise flavors.
3. Call for a gradual or regulated release.
4. In conjunction with anticholinergic drugs.

Excipient selection: The most common excipients used in ODT are lubricants, diluents, at least one disintegrant, and optionally sweeteners, flavoring agents, and swelling agents. The following qualities make bulk excipients ideal for oral disintegrating dosage forms.

1. Disperses and dissolves without leaving any trace in the mouth in a matter of seconds.
2. Provides a pleasing mouthfeel while hiding the drug's unpleasant flavor.
3. Allows for adequate medication loading and is mostly unaffected by temperature or humidity variations(15).

Excipients play a crucial part in the composition of tablets that melt quickly. For quicker melting qualities, the excipients' temperature should ideally be between 30 and 350 degrees Celsius. Table1contains an excipient's detailed list(6).

Table 1: Excipients used for the preparation of ODTs (6).

S.No	Excipients	Function	Example
1	Sweeteners and sugar-based excipients	This is an additional method of producing ODT through direct compression. Excipients with a sugar base serve as bulking agents. They have a pleasant mouthfeel and taste-masking ability due to their high-water solubility and sweetness	Artificial sweeteners like Aspartame, and sugar derivatives. Bulking agents like dextrose, fructose, isomalt, lactitol, maltitol, maltose, mannitol, sorbitol, starch hydrolysate, polydextrose, and xylitol
2	Flavors	Boosts acceptance and compliance in patients	Peppermint flavor, cooling flavor, flavor oils and flavoring aromatic oils, peppermint oil, clove oil, bay oil, anise oil, eucalyptus oil, thyme oil, and oil of bitter almonds. Flavoring agents include vanilla, citrus oils, and fruit essences.
3	Super-disintegrant	accelerates the pace of decomposition by disintegration. Disintegration is accelerated by the addition of additional formulation ingredients such as effervescent agents and water-soluble excipients. The super disintegrant is used to create a tablet with the fast-dissolving property, which is necessary for the tablet to be successful.	Crospovidone, Microcrystalline cellulose, sodium starch glycolate, sodium carboxy methylcellulose, pregelatinized starch, Carboxymethyl cellulose, and modified corn starch. Sodium starch glycolate has better flow ability than croscarmellose sodium.Cross povidone is fibrous in nature and highly compactable.
4	Surface Active agents	Reduces interfacial tension and thus enhances solubilization of FDT.	Sodium dioxide sulfate, sodium lauryl sulfate, polyoxyethylene sorbitan fatty acid and esters (Tween), sorbitan fatty acid esters(Spans), and polyoxyethylene stearates.
5	Binder	Preserve the dose form's integrity before administration	Polyvinylpyrrolidone (PVP), Polyvinyl alcohol (PVA), Hydroxypropyl methylcellulose (HPMC)
6	Lubricant	A lubricating layer is introduced between the mechanical moving elements of a tablet punching machine by lubricant, which helps reduce wear and friction.	Stearic acid, Magnesium stearates, Zinc state, calcium state, talc, polyethylene glycol, liquid paraffin, magnesium lauryl sulfate, Colloidal silicon dioxide.
7	Colour	Improves the dose form's look and organoleptic qualities.	Sunset yellow, Amaranth, Red ironoxide.
8	Fillers	Enhances bulk of dosage form	Directly compressible spray dried Mannitol, Sorbitol, xylitol, calcium carbonate, magnesium carbonate, calcium phosphate, calcium sulphate, pregelatinzed starch, magnesium trisilicate, and aluminium hydroxide.

Table-2: Commercial ODT formulations on the market (10).

Product	Active substance	Company
Maxalt®	Rizatriptan	R.P. Scherer/Merck, Kenilworth,NJ,USA
Zyprexa®	Olanzapine	R.P. Scherer/EliLilly, Indianapolis, USA
PepcidRPD	Famotidine	Merck and Co.,NJ,USA
Zofran®	Ondansetron	R.P. Scherer/GlaxoSmithKline, Philadelphia, PA,USA
Feldene	Piroxicam	PfizerInc.,NY,USA
Risperdal®	Risperidone	Janssen Pharmaceuticals,Beerse, Belgium
Remeron®	Mirtazapine	CIMA/Organon, Oss, Netherlands
Triaminic®SoftChews®	Phenylephrine-dextromethorphan	CIMA/Novartis Consumer Health, Basel, Switzerland
Zelapar™	Selegiline	Amarin Corp.,London,UK

Nimulid-MD	Nimesulide	Panacea Biotech,NewDelhi,India
Romilast	Montelukast	Ranbaxy LabsLtd.,NewDelhi,India
TorroxMT	Rofecoxib	Torrent Pharmaceuticals,Ahmedabad,India
Olanex Instab	Olanzapine	RanbaxyLabsLtd.,NewDelhi,India
Mosid-MT	Mosapridecitrate	Torrent Pharmaceuticals,Ahmedabad,India
Benadryl®	Diphenhydramine	Yamanouchi/Pfizer, Morris Plains, NJ, USA
Claritin® RediTabs®	Loratadine	R.P. Scherer/Schering-Plough, Kenilworth, NJ, USA
Alavert®	Loratadine	CIMA/Wyeth Consumer Health, Madison, NJ, USA
Zomig®	Zolmitriptan	CIMA/Astra Zeneca, Wilmington, DE, USA
Tempra®	Acetaminophen	CIMA/Mead Johnson, Chicago, IL, USA
NuLev.	Hyoscyamine	CIMA/Schwarz Pharma, Milwaukee, WI, USA
Ultram®	Tramadol	JANSSEN PHARMS
Excedrin®	Acetaminophen, aspirin	Ethypharm/BMS, Philadelphia, PA, USA
Febrectal	Paracetamol	Prographarm, France
Adzenys XR-ODT™	Amphetamine (extended release)	Neos Therapeutics
Ambien®	Zolpidem (extended release)	Sanofi Aventis
Cotempla XR-ODT™	Methylphenidate (extended release)	Neos Therapeutics
Dexilant®	Dexlansoprazole (only dual delayed release)	Takeda, Lexington, MA, USA

Methods of preparation of Oro dispersible tablets(15):

1. Molding.
2. Mass extrusion.
3. Spray drying.
4. Cotton candy process.
5. Compaction method.
6. Lyophilization

Formulation method-merits and demerits:

Molding. ODTs made using the molding technique dissolve in 5 to 15 seconds. Heat molding and compression molding are the two categories into which molding, or solid dispersion, can be divided. Molded tablets are made from a molten material that contains a medication that has been dissolved or dispersed. Firstly, the drug is suspended in agar containing water-soluble carbohydrates such glucose, sorbitol, mannitol, lactose, or sucrose. These sugars have the dual function of binding and improving mouthfeel. Subsequently, After the suspension is filled into moulds and blister cases, the solvent is vacuum-evaporated at 30°C to solidify the agar solution and create ODTs(3). Mass extrusion. During the mass extrusion process, water-soluble solvents such as PEG, methanol, or ethanol are used to soften the powder mixture. It is then syringed or sieved through the extruder. Alcohol was eliminated by evaporation following extrusion. The product is a string-shaped gel that solidifies and is then crushed into granules with a mortar. Then, using compaction techniques covered in the ensuing sections, these granules might be combined with additional ingredients to create ODTs. PEG stearate is used as a binder in mass extrusion to enhance disintegration and physical strength. It is possible to mask the bitter taste of the medication by coating the granules with materials such as Eudragit E 100, ethyl cellulose, hydroxypropyl methylcellulose (HPMC), hydroxypropyl cellulose (HPC), polyvinyl alcohol, and polyvinyl acetate(8). Spray drying. Solid dispersions and micronized drug/excipient particles are often manufactured for oral or inhalation administration using the spray-drying process. To create a highly porous structure, a liquid mixture of materials is first sprayed into a heated chamber. These microparticles were then usually combined with mannitol and kneaded with distilled water, followed by a two-hour drying process at 60°C. The produced granules were then sieved, combined with additional excipients, and compacted into tablets using the compaction techniques covered in the sections that follow. This process produces tablets with a high porosity that dissolve quickly in the mouth(16). The main drawbacks of this approach are the product's fragility and high production costs, which render traditional packing techniques unsuitable for this dosage form(6). Cotton-Candy Method. This method uses a unique spinning device to produce crystalline flosses. When saccharides or polysaccharides, such

as poly-maltodextrin and polydextrose, are flash melted and spun simultaneously at a temperature between 180 and 266 degrees Celsius, a candy floss matrix is produced. After that, the produced matrix is compressed into ODTs by milling, blending, and adding API and excipients. This practice is used to mask the unpleasant taste of medications. Furthermore, the flow characteristics, compressibility, and mechanical strength of the candy floss matrix may be somewhat enhanced by partial recrystallization. It also leads to a lot of pharmaceuticals piling up, but it isn't good for thermolabile medications. Freeze-drying, or lyophilization. The process of lyophilization involves using a vacuum to dry thermosensitive active pharmaceutical ingredients at a low temperature. A common term for freeze-dried ODTs is lyophilizates. They often break down quickly, have extremely porous structures, and are very light. Accurate dosage can be achieved by simulating liquid freeze-dried OTDs. Moreover, it is safer for operators to handle strong or poisonous APIs in a liquid form rather than a powdered form. Nevertheless, the procedure is somewhat expensive and inappropriate for formulations that degrade at elevated temperatures and humidity levels(1).

There are two lyophilization platforms: Lyoc and Zydis. The first step in the Zydis process is to create an aqueous bulk liquid with gelatin acting as a polymeric binder and mannitol acting as a mechanical booster. Gelatin serves as a glue to hold the filler and API particles together in the completed ODT. Moreover, disintegration may be aided by the addition of a hydrophilic filler, such as mannitol, which is extremely soluble in water(17). Furthermore, the formulation may contain colorants, pH adjusters, taste-masking agents, and preservatives. The liquid component is then put into blister pockets and rapidly frozen using a tunnel freezer. When fully frozen, blisters are transferred to large industrial batch freeze-dryers for vacuum-assisted primary and secondary drying. Blisters are sealed and stored once they have dried. The medication on this platform has a low dosage, is water insoluble, and has small particles to speed up processing and produce a smooth mouth feel(3). One of Zydis's drawbacks is that intra-batch pore-size variability results from the semicontinuous freezing mode's inconsistent hardening duration. Second, some people cannot consume animal products such as gelatin due to ethical concerns; additionally, the quality of gelatin varies, and its viscosity is affected by temperature, pH, and time. As an alternative to gelatin, polyvinyl alcohol (PVA) has been investigated and documented. As xanthan gum does not prevent drug sedimentation during the initial freeze-drying step, it was chosen as a viscosity enhancer(9). Raman spectroscopy might be used to quantify sedimentation, and xanthan gum content could be adjusted to lessen it. For stability and flexibility during manufacture, polymers like as gelatin, dextran, and alginate are required for the glassy amorphous structure. For example, in the production of terbutaline sulphate ODT, gelatin and sodium alginate were selected as matrix-forming and viscosity modifiers. The formulation also included hydroxypropyl methoxy cellulose, Pluronic F68 (as a surfactant to increase low solubility of TBS), PEG 4000 (as a disintegration accelerator), and mannitol, which gives crystallinity and hardness to freeze-dried ODTs. In order to create homogenous ODTs, simethicone was also used as an antifoaming ingredient because foaming during the mixing process might lead to form variance.(11). With Lyoc technology, water-soluble fillers like lactose or mannitol are used to create an oil-in-water emulsion. When a lot of fillers are used, the formulation eventually becomes paste-like, and sedimentation is prevented. Next, commercial freeze-dryers are used for the freeze-drying stages, just like in the Zydis process. Because of its low porosity and longer drying time, the Lyoc approach was less cost-effective(18), (19).

Compaction Method: During this procedure, a compression device applies pressure to encourage the agglomeration and bonding of particles, preparing integrated structures such as tablets or briquettes(2). The excipient characteristics, APIs, and tablet size all affect the applied compression force. For instance, the study by Stoltenberg and Breitkreutz states that the compression force for ODMT emulation should be between 3 and 8 kN. Another important consideration is the choice of excipient because compression reduces the product's porosity, which is necessary for a quick disintegration and calls for the use of super disintegrates and sugar-based fillers. There are several types of compaction processes, ranging from serial devices like extrusion to limited compression devices like tableting. The compaction approach serves as the foundation for the subsequent methods(3).

Table 3: Conventional techniques used for the preparation of ODTs (3), (20).

S.No	Techniques	Method and characteristics of prepared ODT's
1	Disintegrant addition	Involves adding super disintegrants to the formulation at the appropriate concentration to encourage rapid dissolving or disintegration. For instance, the formulation of oxybutynin and pirenzepine uses crystalline cellulose (AvicelPH-102) and low substituted HPEC, while the formulation of Efavirenz uses MCC and sodium starch glycolate. Used in galanthamine HBr is crospovidone. Prochlorperazine maleate formulation uses cross carmellose Na (5%w/w) and crospovidone (3%w/w). Features: a higher percentage of disintegrants, a lesser hardness, and a higher percentage of friability, much like traditional tablets.
2	Freeze Drying and Lyophilization	The drug is dispersed or dissolved in an aqueous solution of a carrier. The mixture is inserted into the prefabricated blister packets. The trays holding the blister packs are placed through a liquid nitrogen freezing tunnel to freeze the medication solution. The frozen blister packs are subsequently stored in refrigerator cabinets to complete the freeze-drying process. After that, the blisters are packed and shipped. Features: The preparations exhibit enhanced absorption and bioavailability due to their high specific surface area, fast dissolution, and high porosity. Included dose:400 mg insoluble Drug loading soluble in water: 60 mg. Benefits: It offers quick disintegration (5 seconds). It boosts the drug's absorption and bioavailability. For heat-sensitive drugs that contain chemicals that are thermolabile, lyophilization can be helpful. The lyophilized tablets dissolve quickly in less than 5 seconds because saliva enters the pores in the mouth cavity quickly. **Drawbacks:** Process is time-consuming and somewhat costly. The resultant product is unstable, delicate, and sensitive to moisture, making traditional packaging inappropriate. Extremely low physical resistance, high production costs, and low dosage of medications soluble in water.
3	Sublimation	After being combined with the other tablet ingredients, inert solids that volatilize quickly, such as urea, camphor ammonium carbonate, ammonium bicarbonate, and hexamethylenetetramine, are compacted into tablets. Sublimation was then used to eliminate the volatile components, creating a porous structure. **Features:** Porous shape that facilitates better dissolve when a solvent or volatile material, such cyclohexane or benzene, is utilised. **Benefits:** Strong physical resistance and a structure with high porosity Drawbacks: detrimental leftover adjuvant, additional heating apparatus, not suitable for volatile or heat-sensitive medications.
4	Mouling	By using water-soluble ingredients and a hydro-alcoholic solvent, tablets are created at a pressure lower than with conventional tablet compression. Features: The porous nature of compressed tablets increases absorption and facilitates disintegration and dissolution, whereas moulded tablets are much less compact. **Benefits:** Extremely quick disintegration (5–15 s) **Drawbacks:** Exorbitant production costs; poor mechanical strength; potential stability issues.
5	Spray-Drying	By employing hydrolyzed and non-hydrolyzed gelatins as supporting agents, mannitol as a bulking agent, sodium starch glycolate or cross carmellose sodium as a disintegrating agent, and acidic (like citric acid) and/or alkali (like sodium bicarbonate) materials to enhance disintegration /dissolution. Features: When the prepared tablet is submerged in an aqueous media, it dissolves in 20 seconds.
6	Mass Extraction	Involves softening the active blend by using a solvent mixture of water-soluble polyethylene glycol and methanol. After the mass has softened, it is ejected using an extruder or syringe to give the product a cylindrical shape. A heated blade is then used to divide the material into even segments to create tablets. **Features:** The powdered material can be applied to medication granules to cover up their harsh flavour.

7	Direct compression	Direct compression involves standard tools, readily accessible excipients, and a minimal number of processing stages. **Features:** It is the most economical method of producing tablets. **Benefits:** • Processing time and energy consumption are reduced since fewer unit operations are required than with wet granulation. • Less issues with stability for actives that are sensitive to heat or moisture • Compared to wet granulation, direct compression tablet preparation may result in faster dissolution rates for some drugs, such as norfloxacin. • A direct compression formula might require less excipients. **Drawbacks:** Matching the particle size and density of the active medicinal ingredient with excipients can minimize segregation problems. In general, the amount of drug content is limited to approximately 30% or 50 mg. It is not suitable for medicinal compounds with weak flow. During mixing, static charges may accumulate on the drug particles or excipients, which could lead to particle clumping and inadequate mixing.
8	Cotton candy process	Involves spinning and flash melting in tandem to produce a polysaccharide matrix. This candy floss matrix is re-crystallized, crushed, combined with active ingredients and excipients, and compressed to FDT. Characteristics: It provides better mechanical strength and can handle large medication dosages.
9	Compaction Melting granulation Phase transition process	PEG-6-stearate, a hydrophilic waxy binder (super polystate), is added to prepare. Super polystate not only acts as a binder but also facilitates the tablet's disintegration while increasing its physical resistance. **Features:** It dissolves quickly in the tongue and melts, leaving no trace. Produced by heating a powdered mixture of two sugar alcohols with different melting points—to a temperature that is in between that of one with a high melting point and the other with a low melting point. During the heating process, the hardness of the tablet increased because the phase change of lower melting point sugar alcohol caused an increase in interparticle bonding. **Features:** The formulation obtained appropriate hardness and increased compatibility.
10	Nanonization	Involves milling the medication using a patented wet-milling technology to reduce its size to nanosize. **Features:** It works with medications that aren't very soluble in water. Because of its remarkable longevity and broad range of doses (up to 200 mg of medicine per unit), it results in greater bioavailability and dose reduction, a cost-effective manufacturing technique, and standard packaging.
11	Fast Dissolving Films	Involves reducing the drug's size to nanoscale with the use of a patented wet-milling method. The drug's nanocrystals are stabilised against agglomeration by surface adsorption on specific stabilisers prior to being included into ODTs. **Features:** It is used for medications that are not very soluble in water. It results in a more economical manufacturing method, increased bioavailability, dose reduction, and traditional packaging because of its remarkable endurance and broad range of doses (up to 200 mg of medicine per unit).
12	Tableting (standard) Tableting (effervescent) Tableting (humidity treatment)	Benefits: Minimal production costs Utilization of common tools and materials elevated dosage A strong physical barrier. Drawbacks:The size and hardness of the tablets have a big impact on their disintegration quality. Benefits: Use of common equipment, high dosage, good physical resistance, and pleasant effervescent tongue feel. Drawbacks: Operating in controlled low humidity, Requirement of completely impermeable blister Benefits: Strong physical resistance. Satisfying tongue sensation Drawbacks: Additional humidification and drying equipment Potential stability restrictions, exorbitant manufacturing costs, unsuitable for chemicals sensitive to moisture prior to humidity treatment, fragile

Tabel-4: Patented technology and their branded products (2).

S.N	Technology	Process involved	Patent owner	Drug used. (brand name)
1	Zydis	Lyophilization	R.P.Scherer Inc.	Loratidine (Claritin Redi tab and Dimetapp Quick Dissolve)
2	Quick Solv	Lyophilization	Jansen pharmaceutical	Cisapride monohydrate (Propulsid Quicksolv), Risperidone (Risperdal M-tab)
3	Lyon	Compressed tablets	Farmlyoc	Phloroglucinol Hydrate (Spasfon Lyon)
4	Advatab	Microcaps and diffuse cap CR technology	Eurand international	Adva Tabcetrizine, Adva Tab Paracetamol
5	Oraquick	Micromask taste masking	KVPharm.Co.,Inc.	Hyoscyamine Sulphate ODT
6	Flash melt	Moulding	Elan Corp	-
7	Wow tab	Compressed Tablets	Yamanouchi Pharma Technologies,Inc.	Famotidine(GasterD)
8	Rapi tab	Compressed Tablets	SchwarzPharma	-
9	Durasolv	molding	CimaLabsInc.	Hyoscyamine Sulphate (NuLev)Zolmitriptan (ZolmigZMT)
10	Orasolv	Compressed Tablets	Cima LabsInc.	Paracetamol (Tempra Quicklets), Zolmitriptan (Zolmig Repimelt)
11	Flash dose	Cotton-candy process	Fuisz TechnologyLtd.	Tramadol HCl (Relivia Flashdose)
12	zip lets	molding	Eurand	Ibuprofen (Cibalgina DueFast)

Evaluation of ODTs:

Tests and evaluation parameters for the tablets listed in the pharmacopeia's must be evaluated. The quality of the blends' physicochemical properties typically dictates the tablet's quality once a rule is established. Numerous formulation and process variables are involved in mixing, and each one has the potential to affect the final blend's qualities(6).Blend evaluation Before compression: the following properties of blends need to be tested.

Angle of repose: This can be found using the funnel method. The precisely weighed mixture is poured into a funnel. The funnel's height is set such that the tip of the funnel just touches the top of the mix pile. The mixture of medicine (as solid dispersion) and excipient is let to freely pass through the funnel and reach the surface. The following formula is used to determine the angle of repose and estimate the diameter of the powder cone(21).

$\tan\theta = h/r$

Where h and r are the height of the cone and radius cone base respectively. An angle of Repose less than 30 ° shows the free flow of the material.

Bulk density: Pouring a weighed amount of blend into a graduated cylinder and measuring the weight and volume will yield the apparent bulk density. You may compute bulk density using the formula below(3):

Bulk density can be calculated as follows: powder weight/packing volume.

Tapped density(22): This is calculated by filling a graduated cylinder with a known mass of a mixture of drugs and excipients. At intervals of two seconds, the cylinder is allowed to drop under its own weight from a height of 10 cm onto a hard surface. Tapping is kept up till the volume doesn't change anymore.

The formula for calculating tapped density is as follows:

Tapped Density = (Weight of the powder/volume of the tapped packing)

Compressibility index: The Compressibility Index of the blends is determined by the compressibility index. The Compressibility Index can be calculated by using the following formula(7):

Compressibility Index(%)=[(TD-BD)X 100]/TD]

Hausner's ratio: Hausner's ratio can be used to define an index that is comparable to show the flow qualities. This formula can be used to compute Hausner's ratio(6).
Hausner's ratio = (Tapped density x 100)/(Poured density)
Hausner's ratio <1.25–Good flow=20% compressibility index
1.27–Poor flow=33% compressibility index
Void Volume: The volume of the spaces is known as the void volume "V" and is given by the formula (21).
V=Vb–Vp
Where,Vb=Bulk volume (volume before tapping) Vp=True volume (volume after tapping)
Porosity: The porosity € of powder is defined as the ratio of void volume to the bulk volume of the packaging. The porosity of the powder is given by the following formula(9):
€ =Vb–Vp/Vp=1-Vp/Vb
Porosity is frequently expressed in percentage and is given as:
%€=(1– Vp/Vb)X100
The porosity of powder indicates the types of packaging a powder undergoes when subjected to vibrations, when stored, or in a tablet machine when passed through the hopper or feed frame.
Evaluation of Tablets: All the formulated ODTs are subjected to the following quality control tests.
Weight variation: To make sure that the weight of the pills in a batch is consistent, the weight variation test is conducted. First, the average is computed based on the total weight of 20 pills from each formulation. To ascertain the weight variance, the weight of each tablet is also ascertained individually(6).
Hardness: The hardness of a tablet indicates its strength. To test the tablet, find the force required to split it in half lengthwise. A hardness of approximately 3-5 kg/cm2 is considered sufficient for uncoated tablets, with force measured in kilograms. Ten pills from each formulation are subjected to a hardness test by Monsanto and other hardness testers to measure the hardness (20).
Friability test: Friability is defined as the weight loss of the tablet inside the container because of surface fine particle removal. Determining the tablet's resistance to abrasion during handling, packing, and transportation is the goal of the friability test. The tablets' friability is assessed using the Roche friabilator. Each batch of 20 tablets should be weighed before being placed in a Roche friabilator and rotated at 25 rpm for four minutes. After dusting every tablet, reweigh. The following formula can be used to determine the percentage of friability(15):
%Friability=[(W1-W2)100]/W1
Where, W1= weight of the tablet before the test, W2= weight of the tablet after test
Disintegration test: Six glass tubes, each measuring three lengths, with an open top and a ten-inch screen at the base of the basket rack assembly, are part of the USP disintegration equipment. Each tube has one tablet, and the basket rack is contaminated with one liter of distilled water at 37± 2 °C. The tablets should stay below the liquid's surface during their upward motion and not come any closer to the beaker's bottom than 2.5 cm(3).
Mechanical strength: Tablets need to be strong enough to withstand handling shocks throughout production, packing, and delivery. Two crucial factors in determining mechanical strength are friability and crushing strength. Tablet or Smashing Power It is important to keep in mind that an excessive amount of crushing strength will reduce the disintegration duration. Tensile strength is the amount of force required to compress a tablet in a radial direction and break it. Pfizer hardness testers are used to measure the tablet's crushing strength. The equation is used to compute the tensile strength for crushing (T)(5):
T=2F/ π*d*t
Where F is the crushing load, and d and t denote the diameter and thickness of the tablet respectively.
Uniformity of dispersion: For two minutes, keep the two pills in 100 milliliters of water and mix gently. 22 meshes are used to pass the dispersion through. If there is no longer any residue on the screen, the tablets will be deemed to have passed the test.(5).
Wetting time: There is a straightforward method for measuring the wetting time of the pill. Place the five circular tissue papers of 10 cm diameter in a Petri dish containing 0.2% w/v solution (3ml). A tablet is carefully placed on the surface of the tissue paper. The time required to develop a blue color on the upper surface of the tablet is noted as the wetting time(12).
Water absorption ratio: Six milliliters of water are contained in a small Petri dish with a little piece of tissue paper folded twice inside. Place a tablet on the paper, and note how long it takes for it to get completely wet. Next, reweigh the moist tablet. The following formula is used to find the water absorption ratio, or R(6).
R=100xWa-Wb/Wb

Where Wb is the weight of the tablet before water absorption
Wa is the weight of the tablet after water absorption.

Taste and feeling in the mouth: Patients should be given a product that has a pleasing mouthfeel since this is important. Each batch of tablets has one tested pill that is placed on the tongue to gauge feeling. The mouthfeel is assessed on human volunteers who are in good health. Five members of a panel evaluate tastes using the time intensity approach. 40 mg of the sample, or one dose of the medication, is placed in the mouth for 10 seconds, and the taste is recorded immediately; this is repeated 1, 2, 4, and 6 minutes later. The flavor is evaluated by the volunteers using a scale of 0 for excellent, 1 for tasteless, 2 for mildly bitter, 3 for bitter, and 4 for terrible(6).

In-vitro disintegration: To find the in-vitro disintegration time, a tablet is dropped into a beaker containing 50 milliliters of pH 6.8 Sorenson's buffer. Three tablets are selected at random for each formulation, and the in vitro dispersion time is recorded.

In-Vivo disintegration test: Two or three pills are used in the test, and the amount of time it takes for the tablets to completely dissolve in the mouth is measured in seconds(11).

In-vitro dissolution test: The USP Type II apparatus (Paddle type) is used to perform in-vitro dissolution studies at a speed of 50 rpm. The dissolution medium, 900 cc of phosphate buffer pH 6.8, is kept at 37±0.5°C. At predetermined intervals of time (2 minutes), remove an aliquot of the dissolving medium (10 ml) and filter. Appropriate analytical techniques are used to determine the amount of medication that dissolves(2).

Stability Studies: In accordance with ICH recommendations, the optimised formulation of ODTs is put through a stability study to evaluate the stability of their physical features and release attributes(1).

CONCLUSION

Oral disintegrating tablets exhibit greater patient acceptance and compliance in comparison to conventional oral dose forms. Additionally, there may be possible advantages in biopharmaceutical characteristics, efficacy, and safety. Prescription ODT medicines were first created to help patients with dysphagia—disability swallowing conventional tablets—who were young, old, and mentally ill. ODTs are now more extensively accessible as over-the-counter (OTC) medications to treat allergies and symptoms of the flu and colds. To accomplish fast disintegration and immediate dissolving of the tablet together with superior flavor masking properties and high mechanical strength, ODTs should incorporate super disintegrating agents at the ideal concentration and optimize the tablet matrix's porous structure. Many medications, particularly unpleasant drugs, can be included in ODT. The investigation is still ongoing. Water can penetrate the core of novel multichannel ODTs, which has solved the disintegration issue. Solvent-free granulation and suspension techniques could be useful in addressing environmental problems. Moreover, melt-granulated particles are economical and have a regulated release. New pharmaceutical excipient developments should be expected, as should future advancements in ODT technology.

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