Advances in Bioresearch
Adv. Biores., Vol 14 (2) March 2023: 213-223

Print ISSN 0976-4585; Online ISSN 2277-1573
Journal's URL:http://www.soeagra.com/abr.html
CODEN: ABRDC3
DOI: 10.15515/abr.0976-4585.14.2.213223

Advances in Bioresearch

REVIEW ARTICLE

Orally Disintegrating Tablet: A Revolutionary New Drug Delivery System

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ABSTRACT
Oral medications have been the most popular way to deliver medications to patients and maintain their health for decades. The oral route of delivery has been a dominant one for the delivery of medications over time.Nevertheless, while pills and capsules have been an effective delivery mechanism, they have limitations. However, today, there's a better way to get medications into the body: Orally disintegrating tablets,also known as ODTs. These tablets are a revolutionary system for drug delivery that provides patients with the convenience & flexibility of oral delivery without the drawbacks of pills and capsules. The first orally disintegrating tablet was introduced in the early 1980s. These tablets have shown much promise as a means of delivering drugs. In, this article, we will explore what ODTs are, how they work, their preparation methods and technologies, and why they are such a game-changer for medication delivery and its future perspectives. We will also explore some of today's most popular orally disintegrating tablets.
Keywords: ODTs, Drug Delivery System, CDER

Received 04.02.2023 Revised 16.03.2023 Accepted 25.03.2023

How to cite this article:
Tangku Lepcha, Kavitha A N. Orally Disintegrating Tablet: A Revolutionary New Drug Delivery System. Adv. Biores. Vol 14 [2] March 2023. 213-223

INTRODUCTION

Orally disintegrating tablets (ODTs) are a novel drug delivery system currently being investigated to improve the bioavailability of drugs. The ODT is a tablet that disintegrates in the mouth, releasing the drug into the oral cavity and rapidly absorbed into the systemic circulation. The ODT is not a new formulation, but a variation on a tablet has been used to disperse other formulations in the oral cavity [1].One of the major differences between the ODT and other tablets is that the ODT is designed to dissolve rapidly in the mouth, allowing the drug to be released into the oral cavity and absorbed into the systemic circulation. The ODT has been a topic of much discussion in the pharmaceutical community as a novel drug delivery system, as it has the potential to change the way medications are administered and prescribed.

After the Agency received and reviewed applications for the initial ODT products, the Center for Drug Evaluation and Research (CDER) Nomenclature Standards Committee developed a definition for an ODT in 1998: "*A solid dosage form containing medicinal substances which disintegrates rapidly, usually within a matter of seconds, when placed upon the tongue"*[2]. ODTs are tablets that provide the rapid dissolution of solid to present as a suspension or solution even when placed in the mouth under limited bio-fluid conditions. One of the main advantages that ODTs offer is that they provide a solution for populations with difficulty swallowing. Dysphagia (swallowing difficulties) is common among all age groups, including children. It is more common among pediatric, geriatric, and institutionalized patients and patients with nausea, vomiting, and motion sickness complications [3].ODTs with good taste and flavor increase the acceptability of bitter drugs, making these drugs more accessible to a broader range of people. Orally disintegrating tablets with enhanced taste and flavor are ideal for pediatric, geriatric, institutionalized, and patients with nausea, vomiting, and motion sickness. ODTs are also called as "orodispersible tablets," "mouth dissolving tablets," "melt-in-mouth," "fast-dissolving drug delivery," "rapimelts tablets, "and "porous tablets," "quick-dissolving tablets," etc. [4].

Catalent Pharma Solutions from the U.K, Cima Labs and Fuisz Technologies from the U.S, and Takeda Pharmaceutical Company from Japan were the first three companies to initiate the development of ODTs. The first ODT form of a drug to get approval from the U.S. Food and Drug Administration (FDA) was a Zydis ODT of Claritin (loratadine) in December 1996 [5].

CHARACTERISTICS OF ODTS

ODTs shouldbe able to disintegrate inside the mouth rapidly, preferably less than 40sec without water.

- ❖ It should have a pleasant mouth feel.
- ❖ ODTs should provide optimal compatibility with development technology, including taste-masking and other excipients[6].
- ❖ After the oral administration of the drug, they should leave no residue or minimal residue.
- ❖ ODTs should be strong enough to withstand the manufacturing process and post-manufacturing handling [7].

Mechanism of ODTS

ODT adopts the following mechanisms to achieve the dissolving of a substance very quickly, which results in the desired fast-dissolving characteristics:

1. The tablet matrix must quickly accommodate water to cause rapid disintegration and instantaneous dissolution [8].
2. Highly water-soluble excipients or super-disintegrating agent is incorporated into the formulation.
3. The tablet is broken down into smaller particles, which results in the conversion of solution or suspension form of the drug following the given mechanisms: [9]
   - The high swelling ability for disintegration
   - Chemical reaction
   - Capillary action

Advantages of ODTs One of the major advantages of the ODT formulation is that it provides a combination of both liquid and conventional tablet formulations, making it quick and easy to use.

1. ODT makes it easier for the patients to take tablets as solid dosage forms for a long time and avoid ingestion of liquid.
2. More easily and quickly dissolve in the oral cavity and are easily absorbed by the gastrointestinal tract.
3. ODTs formulation allows high drug loading.
4. It dissolves without leaving any residue in the mouth.
5. Better stability, an easier production process, and a smaller packaging size are more accessible to the patients [10].
6. They are easy to transport, carry and store.
7. No difficulties in administrating to children, old, and mentally challenged patients.
8. ODT gives more accurate dosing than liquid formulation.
9. They are more stable than liquid dosage forms and are excellent for long-term storage.
10. The dissolution and absorption rate of the drug is quick, which offers a rapid onset of action.
11. Some drugs are absorbed through the mouth, pharynx and esophagus through saliva, which then transfers to the stomach and increases bioavailability [11].
12. They are convenient for smaller packaging sizes due to the solid tablet forms and more straightforward production process.

Disadvantages of ODTs

- **i.** One disadvantage of ODTs is that they are fragile and difficult to handle because they are compressed into tablet form with low compression.
- **ii.** Taste masking is one of the biggest challenges in ODTs as bitter drugs cannot be formulated into ODTs.
- **iii.** ODTs need specialized packing materials due to their hygroscopic nature.

Ideal Drug Candidate for ODTs[12]

Several factors must be considered when selecting drug candidates for ODT dosage forms.

- ✓ The drug must be palatable.
- ✓ The dose of the drug has to be lower than 20mg.
- ✓ The drug should have low to moderate molecule weight.
- ✓ The drug should have the ability to diffuse and partition throughout the epithelium of the upper GIT (logP>1, or preferably>2).
- ✓ The drug has to be partially non-ionized at the oral cavity pH.
- ✓ The drug should be able to permeate through oral mucosal tissue.

- ✓ The drug should have pre-gastric absorption properties.
- ✓ The drug should have excellent stability in both water and saliva.

Excipients Used in the Manufacturing of ODTs[13]

Excipients are essential parts of pharmaceutical drugs. The selection of excipients is mainly based on their compatibility with the active pharmaceutical ingredients. A pharmaceutical product's excipients can perform various roles during the formulation. Excipients are used not only for increasing the bulk of the formulation but also for various functions such as stabilizing, protecting, identifying, delivering, and increasing the patient compliance to the drug. The main types of excipients used in ODTs are super disintegrants, diluents, lubricants, surface-active agents, binders, fillers, sweeteners, and flavors.

Table No. 1 Examples of Excipients used in ODT

Types of Excipients	Examples	Application
Super-disintegrant	Crospovidone	Water-insoluble tablet disintegrant and dissolution agent used at 2–5% concentration in tablets.It can also be used as a solubility enhancer.
	Croscarmellose	These tablet disintegrants at 0.5-5% concentration and capsule disintegrants at 10-25% concentration.
	Sodium Starch Glycolate	Disintegration occurs by the rapid uptake of water followed by rapid and enormous swelling with a usual concentration between 2-8%.
	Modified Corn Starch	Starches absorb water rapidly, allowing tablets to disintegrate appropriately.
	Carboxy Methylcellulose Sodium	Produces thixotropic gels suitable for suspending vehicles in pharmaceutical andcosmetic formulations.
Surface-Active Agents	Sodium Lauryl Sulphate	It is an anionic surfactant. It is also used as a detergent and wetting agent effective in alkaline and acidic conditions.
	Polyoxyethylene Sorbitan Fatty Acid Esters	Hydrophilic nonionic surfactants are typically used as emulsifying agents to prepare stable oil-in-water pharmaceutical emulsions on a commercial scale.
	Sorbitan Fatty Acid Esters	Lipophilic nonionic surfactants are mainly used as emulsifying agents during the formulations of the dosage form.
	Polyoxyethylene Stearates	Used as anemulsifying agent and blended with surfactants to obtain hydrophilic-lipophilic balance.
Diluents	Magnesium Carbonate	They are used as a directly compressible tablet diluent in concentrations up to 45% w/w.
	Calcium Sulfate	In granular form, it has good compaction and moderate disintegration properties and is used in the formulation of tablets and capsules.
	Magnesium Trisilicate	Used in oral pharmaceutical formulations and food products as a glidant and therapeutically as an antacid.
Binders	Polyvinylpyrrolidone	As a binder, PVP is used in the concentration range of 0.5%–5% w/w.
	Polyvinyl Alcohol	It is used as a stabilizing agent in the concentration range of 0.25–3.0% w/v. Polyvinyl alcohol is also used as a viscosity-increasing agent.
	Hydroxypropyl methylcellulose (HPMC)	HPMC refers to soluble methylcellulose ethers and is used as a thickening agent, binder, film former, and hydrophilic matrix material.
Lubricants	Stearic Acid	Mainly used as a lubricant in tablet and capsule formulation.
	Magnesium Stearate	It is primarily used as a lubricant in capsule and tablet manufacture at concentrations between 0.25% and 5.0% w/w.
	Zinc Stearate	They are used in pharmaceutical formulations as a lubricant in tablet and capsule manufacture at concentrations up to 1.5% w/w.
	Calcium Stearate	They are used as a lubricant in tablet and capsule manufacture at concentrations up to 1.0% w/w. However, it has good ant adherent and lubricant properties.
	Talc	Used as lubricants in the formulation of tablets at the concentration range of 1.0-10%.

Taste Masking Technologies

Taste masking is considered one of the most important components in successfully developingan oral solid dosage form. ODTs are often made palatable by masking the bitter taste of their active pharmaceutical ingredients, which is one way to assess their palatability. Following technologies do the taste masking of active ingredients:

Table No. 2 Taste Masking Technologies

SL No.	Taste Masking Technology	Method	Examples
1	Coating	Coating technology was based on type of coating material, coating solvent system, and the number of coating layers. Coating materials such as hydrophobic polymers, lipids, sweeteners, and hydrophilic polymers, either single or combination, and as single or multi-layer coat [14].	Cellulose acetate (CA), polyvinyl pyrrolidone, sucrose, methyl methacrylate, etc.,
2	Granulation	Dry, wet and melt granulation techniques can process mixture of bitter medicaments with sweeteners, hydrophobic polymers and waxes to complete the process of taste masking in solid and liquid dosage forms.	Sugar alcohol, alginic acid, cyclodextrin, microcrystalline cellulose(MCC), polycarbophil, etc.,
3	Sweeteners	Uses of sweeteners in the taste masking technology is the most common technology. It can also be used with the combination of other technologies. Two types of sweeteners are available: natural sweeteners and synthetic sweeteners[15].	Sucralose, aspartame, stevia, saccharine sodium, glycyrrhizin, acesulfame potassium, etc.,
4	Microencapsulation	It is the technique in which the materials are protected from volatilizing, oxidation and masking their taste which works on the principle of solvent extraction and evaporation.	Microencapsulation by ethyl cellulose (EC) with a further coating by a layer of acrylic polymer.
5	Taste Suppressants & Potentiators	Taste Suppressants compete with bitter substances to bind with G-coupled protein (GPCR) receptor site or interact chemically with taste receptors. Potentiators amplify the approach of the taste of sweeteners and mask the unpleasant after taste of bitter substances[16].	Mixture of eucalyptol and methyl salicylate was used in the taste masking of thymol. Thaumatine, neohespiridine dihydrochalcone, glycyrrhizin, etc., are used as potentiators.
6	Solid Dispersion	Solid dispersions were introduced recently in the taste masking technology which works on the principle of drug-polymer matrix composition to achieve taste masking of the bitter drug.	Methacrylic acid copolymer and phthalate polymer are used for the taste masking of cefuroxime axetil.
7	Ion- Exchange Resin	Ion exchange resins are high molecular weight polymers with cationic and anionic functional group. The oppositely charged residues of the resin substrate leads to the adsorption of resin on the drug resulting in the masking of bitter taste with no after taste.	Ion exchange resins like amberlite was used to formulate taste masked fast dissolving orally consumable films of dextromethorphan.
8	Viscosity Enhancers	Viscosity enhancers delays the migration of dissolved medicaments from the surface of the solid particles to the suspending medium and also decreases the contact between bitter medicaments and the taste receptors.	Xanthan gum, microcrystalline cellulose, Hypromellose, sodium carboxymethylcellulose, etc.,
9	Complex Formation	Complex formation has two possible mechanisms either the cyclodextrins wraps the bad tasting molecule to inhibit its interaction with the taste buds, or it interacts with the gate keeper proteins of the taste buds.	Cyclodextrin was used to achieve taste masking of levosulpiride by complex formation.
`10	pH Modifiers	pH modifying agents can generate the specific pH environment that can ease the precipitation of bitter drugs, reducing the overall taste sensation for liquid dosage forms[17].	L-arginine maintains alkaline pH of the suspending vehicle to promote in situ precipitation of des-quinolone in saliva

Methods Used for Preparation of ODTs

Various methods are currently used in preparation of fast disintegrating/dissolving tablets.

Direct compression:

The technique uses a conventional compression machine with common excipients, and it has a limited number of processing steps. Microcrystalline cellulose (MCC) and hydroxypropyl cellulose (HPC) is used to formulate the tablets that disintegrate quickly. Adding effervescent material in a tablet formulation helps disintegrate and mask the taste of the drug rapidly. Super disintegrants such as sodium starch glycolate, crospovidone, alginic acid, calcium silicate, and croscarmellose help in dispersibility with a pleasant feeling. Direct compression is cost-effective, but it can result in low hardness if the tablets have a high amount of disintegrants.

Freeze-drying or lyophilization:
It is a pharmaceutical processing technique thatuses sublimation for dry heat-sensitive drugs by removing water with a vacuum. Drugs are dissolved in an aqueous solution and placed in pre-formed blister packs. Nitrogen is flushed through the packs to freeze the drugs, which are placed in the refrigerator to complete the process. The formulation is highly porous and has a high specific surface area, which allows it to dissolve quickly in the mouth, resulting in high drug bioavailability. This system is high-cost, time-consuming, and fragile, so conventional packing is not appropriate for packing this dosage form. This system also has stability issues under stress conditions, so it is unsuitable for packaging the dosage form[18].

Molding method:
In this technique, the powder mass is dissolved in a hydroalcoholic solvent and then formed into a dosage form, and the solvent is evaporated. The taste enhancement of the drug is developed by spray congealing the molten mixture of hydrogenated cottonseed oil, sodium carbonate, lecithin, polyethylene glycol with an active ingredient, and lactose into tablets. Solvents used in the drying process in this method can leave a porous mass behind, which would promote rapid dissolution.

Sublimation:
To increase the dissolution and disintegration rate, solid volatile ingredients are used in this technique, such as urea, camphor ammonium carbonate, ammonium bicarbonate, and hexamethylene-tetramine. The volatile material will become porous when it is exposed to lower pressure and a slight heat.

Spray-drying:
In a spray-drying process, ingredients are combined by hydrolyzed and non-hydrolyzed gelatins as supporting agents, mannitol filler as a bulking agent, and glycine or croscarmellose sodium as a disintegrating agent in accordance with the applicable pharmacopeia. An acidic material (e.g., citric acid) and alkali (e.g. sodium bicarbonate) enhance disintegration and dissolution. One of the main advantages of the spray-drying method is that it gives rapid dissolution (within 20 seconds), which is important for fast-acting delivery. When the dosage form gets in contact with an aqueous medium, it dissolves almost instantly

Mass-extrusion:
In this method, the mixed ingredients are softened by water-soluble ingredients, such as polyethylene glycol, using methanol as a solvent. They are passed through an extruder to form thin cylinders, whichare cut into small tablets with heated blades. The main approach of this type of method includes the taste masking of bitter drugs by the final product, making smaller granules, thus enhancing oral bioavailability.

Cotton candy process:
This method uses a matrix of polysaccharides to produce a spinning yarn. It is prepared by simultaneous action of melting and spinning. This candy floss matrix is subsequently recrystallized, milled, mixed with an active drug and an excipient, and then compacted to form a fast-dissolving tablet. This type of method is highly suitable for administering large doses, as it can be accommodated in the dosage formwith high mechanical strength.

Nanonization:
In this case, the particle size reduction to nano-size is accomplished by wet grinding.The nano-sized crystalline particles are then stabilized to prevent agglomeration by physical attachment to the surface of inert material. Characteristics of this technique include a suitable dosage range, a cost-effective process, and are suitable for water-insoluble drugs with low bioavailability. It can withstand several types of stress and can withstand large-scale production.

Compaction:
Melt granulation is made by combining hydrophilic waxy binder (super polystrate) PEG-6- stearate. This binder includes dual-action, increasing physical strength while enhancing the tablet's disintegration. The results from these formulation techniques allow for a preparation to be created that melts in your mouth quickly and leaves no residue.

Phase-transition method:
This technique involves mixing and compressing the mixture containing two sugar alcohols: one with a high melting point and the other with a low melting point. We then heat the mixture between the melting points of the two sugar alcohols, which causes the bondages between the molecules to be amplified and the resulting tablet to harden. This method can resist the extreme conditions of manufacturing and shipping and is suitable for use in these scenarios. Hardness is gained during heating, but heat unstable drugs don't work well at this temperature [19].

Different Patented Technologies used in ODTs

ODT,a new drug delivery system that dissolves quickly, has become popular and accepted in recent years. New technologies have been developed to improve existing ones, and research is ongoing to improve preparation methods globally. The examples of marketed ODTs are mentioned in Table NO.4. Some of the developed patented technologies are listed below in Table No.3.

Table No. 3 Patented Technologies used in ODTS

Technology (Patents)	Preparation techniques	Advantages
Zydis (R.P. Scherer, Inc.) **First mouth dissolving tablet**	Freeze drying	Maintain strength during handling Increased bioavailability A substantial amount of pre-gastric absorption
Orasolv (Cima Labs, Inc.) **Effervescence tablet**	Low Compression	Tablet matrix gets dissolved in less than one minute, leaving coated drug powder Drug powder and effervescence help in taste masking[18]
Durasolv (Cima Labs, Inc.)	Compression	Quick dissolution avoids some of the sandy or gritty texture Low friability Disintegration time less than 60 s.
Orodis technology	Compression	Fast disintegration time (15 to 30 s) Hard tablets are easy to handle
Melt Ease technology	-	Tablet dissolution within 5s Available for both children and the elderly Marginal development cost
Quick Dis technology (Lavipharm laboratories) Intraoral fast-dissolving drug delivery system thin, flexible, and quick-dissolving film	-	Available in various packaging configurations, such as unit-dose pouches and multiple-dose blister packages
Wowtab (Yamanouchi Pharma Technologies)	Compression	A combination of tolerable hardness and fast dissolution rate.
Flashdose (Fuisz Technologies, Ltd)	Compression	fast dissolution
Flashtab (Ethypharm, Saint Cloud)	Wet or dry granulation method and followed by compression	A combination of Shear form and Reform technologies is used for taste masking of bitter drugs.
OraQuick (KV Pharompressionmaceuticals)	Compression	It uses microsphere technology, which uses taste masking to provide superior mouth feel, significant mechanical strength, and quick disintegration/dissolution of the product[19].
NanoCrystal (Elan)	Wet milling technique	The rate of the tablets dissolving increased. The tablets were made of nanomaterials, which will dissolve quickly. Extraordinary strength. Wide range of doses (up to 200 mg of active pharmaceutical ingredient per unit).
Dispersible tablet technology	Compression	This will disintegrate within 60 seconds in contact with water when exposed at ambient temperature[20].
AdvaTab technology (Kyowa Hakko Kogyo (Tokyo, Japan))	Compression	30-40 % stronger than conventional tablets. Very hard and durable tablets
Pharmaburst technology (SPI Pharma, New castle)	Compression	Dissolves within 30-40 s.
Frosta technology (Akina)	Compression	Strong tablets with high porosity. Higher strengthened faster disintegration time.
Lyo (Pharmalyoc)	Freeze-drying	Decreased porosity

Some of the marketed ODTs products

Tablets and capsules are considered the most accepted dosage form, and dysphagia is one of the biggest challenges faced in these dosage forms. To overcome this challenge, a new dosage form is being

developed, ODTs. Due to the high degree of patient satisfaction, ODTs are used in the place of traditional tablets and capsules. Over the recent years, ODTs have become one of the highly successful commercial products. Some examples of available marketed ODTs products are listed in Table 4.

Table No.4 Examples of marketed ODTs products[20]

Sl No.	DRUG NAME	BRAND NAME	CATEGORY
1	Alprazolam	Niravam	Benzodiazepines
2	Amphetamine	Adzenys XR	Stimulants
3	Aripiprazole	Abilify	Atypical antipsychotics
4	Clozapine	Fazaclo	Atypical antipsychotics
5	Desloratadine	Clarinex	Antihistamines
6	Donepezil Hydrochloride	Aricept	Cholinesterase inhibitors
7	Lamotrigine	Lamictal	Anticonvulsants
8	Lansoprazole	Prevacid	Proton pump inhibitors
9	Loratadine	Claritin RediTabs	Antihistamines
10	Methylphenidate	Cotempla	CNS Stimulant
11	Metoclopramide Hydrochloride	Metozolv	GI Stimulant
12	Mirtazapine	Remeron	Tetracyclic Antidepressant
13	Olanzapine	Zyprexa Zydis	Atypical antipsychotics
14	Ondansetron Hydrochloride	Ondansetron Hydrochloride	5HT3 receptor antagonist
15	Phentermine Hydrochloride	Suprenza	CNS Stimulant
16	Prednisolone Sodium Phosphate	Orapred	Glucocorticoids
17	Risperidone	Risperdal	Atypical antipsychotics
18	Rizatriptan Benzoate	Maxalt-MLT	Antimigraine agents
19	Vardenafil Hydrochloride	Staxyn	Impotence agents
20	Amlodipine Besylate	Norvasc	Calcium channel blockers
21	Lamotrigine	Lamictal	Triazine-anticonvulsants
22	Vardenafil Hydrochloride	Staxyn	Impotence agents
23	Cetirizine HCl	Zyrtec Allergy	Antihistamine
24	Aripiprazole	Abilify	Atypical antipsychotics
25	Meloxicam	Qmiiz ODT	Nonsteroidal anti-inflammatory drugs

Evaluation of ODTs[21, 22]
The following methods can evaluate tablets:

Table No. 5 Evaluation Parameters of ODT

SL No.	Official Method	Unofficial Method
1	Weight Variation	General Appearance
2	Hardness	Size and Shape
3	Friability	Organoleptic Property
4	Content Uniformity	Tensile Strength
5	Disintegration Test	Moisture Uptake
6	Dissolution Test	Wetting and Water Absorption

1. **Weight Variation:** The USP weight variation test is used to determine the variability of each unit of a pharmaceutical product as determined by 20 individual tablets being weighed, and the average weight is then calculated and compared to the individual weights of the tablets.The tablets meet the USP test if

   "*Not more than two tablets are outside the percentage limit, and if*
   No tablet differs by more than 2 times the percentage limit."

   The % deviation is calculated by using the formula:

$$\%\ Deviation = \frac{Individual\ weig\square t - Average\ weig\square t}{Average\ weig\square t}\ X\ 100$$

Table No.6 Limits for Weight Variation

The average weight of the tablets	%Deviation
80mg or less	±10
80mg to 250mg	±7.5
250mg and more	±5

2. Hardness: The hardness of the tablet is defined as the force required in the order to break the tablet, which is applied across the diameter of the tablet. The hardness of tablets can be determined by using Monsanto hardness tester, Pfizer hardness tester, and another similar hardness tester. The force is measured in kilograms, and the hardness of about 3-6Kg/cm^2 is considered satisfactory.

Table No. Limits for Hardness of Tablets

SL No.	Types of Tablets	Limits
1	Tablet	4-10kg
2	Chewable Tablet	3kg
3	Sustained Release Tablet	10-20kg

3. Friability: Friability is the ability of a tablet to withstand mechanical stress. The Roche friabilator is an instrument that utilizes the principle of centrifugal force. The tablets are placed in the chamber and are dropped at a distance of 6 inches with each rotation. The chamber is revolved at a speed of 25 rpm and rotated for 4mins.

Percentage friability is determined by using this formula:

$$\text{Friability (\% loss)} = \frac{(w1-w2)}{w1} \times 100$$

Limits: It must be **≤ 1%**

4. Content Uniformity: The primary aim of the content uniformity test is to ensure that tablets contain the exact amount of active pharmaceutical ingredients to meet the product's performance specifications. For tablets and capsules of 50mg or smaller, there is a uniformity test for the content of tablets and capsules included in the monographs.

Acceptance limits:

- The content must comply with the requirements if each content is 85- 115% of the average content (i.e, ± 15 %).
- The test fails to meet the standards if more than nor if one individual content is outside the specified range of 75-125% of the average content.
- Suppose one particular content is outside the range of 85 - 115% of the average content but within the 75-125% range. In that case, it will be repeated using 20 different tablets in order to achieve a more accurate determination.

5. Disintegration Test: The disintegration test will be carried out using the apparatus specified in I.P.-1996 (the official document) with randomly selected 6 tablets using distilled water as disintegration media at 37°C.Disintegration time for randomly selected 6 tablets will be measured using disintegration test apparatus. The average time required for disintegration will be calculated and compared with standards.

Acceptance Limit for ODTs: Disintegrate within 1minute.

6. Dissolution Test: The dissolution conditions for drugs listed in a pharmacopoeia can be a good start when trying to identify a drug whose dissolution profile is bioequivalent to the reference drug. ODT should be evaluated for 0.1 M HCl and buffer (pH 4.5 and 6.8) in the same way as its ordinary tablet counterparts. The USP 2 paddle, the most suitable and common apparatus, is used to disintegrate tablets with a paddle speed of 50 rpm orally.

7.Moisture Uptake: As many excipients are hygroscopic, to ensure the stability of the formulation, moisture content studies should be conducted for ODTs. 10 samples from each formulation are stored in a desiccator over calcium chloride at 37°C for 24 hours. Next, the tablets are then weighed and exposed to 75% RH at room temperature for two weeks. One tablet as control: the tablet that does not have super disintegrants is kept assessing the moisture uptake due to other excipients. Over three days, the required humidity(75%RH) is achieved by maintaining saturated sodium chloride solution at the desiccator's bottom. The weight of the tablets is recorded, and the percentages of increase in weight are recorded.

8. Wetting and Water Absorption: The wetting time of a dosage form is related to the contact angle with which the tablet's surface is wetted. A lower contact angle will result in a quicker uptake of fluid by the tablet, which will then cause a faster disintegration. To test the tablet, a tablet is placed on a piece of tissue paper folded twice and kept in a small Petri dish (D = 6.5 cm) containing 6 ml of water, and the time for complete wetting is measured.

9. Organoleptic Property: The color should be consistent and show no signs of discoloration. The color of the tablet should match the standard color.

10. Size and Shape: The tablet's size, shape, and dimensionality can be described and monitored. Tablet thickness is one of the important features in the reproduction of appearance and in the use of filling

equipment. Some tablet filling equipment utilizes the uniform thickness of the tablets as a counting mechanism. Ten tablets were taken, and their thickness was recorded using a micrometer.

11. Tensile Strength: Crushing strength is also known as tablet tensile strength. It is the force required to break a tablet in the radial direction and the force required to break a tablet in the tangential direction. It is important to note that excessive crushing strength significantly reduces the tablet's disintegration time. Pfizer hardness tester is used to measure the tensile strength of the tablet. Tensile strength for crushing (T) is calculated using the equation

$$T = 2F / \pi \times d \times t$$

Where F is the crushing load
d is the diameter of the tablet
t is the thickness of the tablet.

CHALLENGES AND LIMITATIONS OF ODTS

ODTs have achieved a wide range of acceptance in the field of the pharmaceutical industry with their advantages over conventional dosage forms. However, it also has their own sets of challenges. The biggest challenges in formulating and manufacturing ODTs are their physio-mechanical properties, taste-related properties, drug molecule, sensitivity to environmental conditions, and cost [23].

To disintegrate and swallow, ODTs are made of porous or soft molded matrices, making them fragile structures requiring peel-off blister packing, thus increasing their cost. Drug properties significantly affect formulation parameters, affecting manufacturing methods and, ultimately, the final properties of the tablet. The colloidal nature of ODTs requires different manufacturing techniques, which must be determined considering the specific drug properties. For example, ODTs are sensitive to environmental conditions, which require special packaging, handling and processing techniques. In addition, they are prone to oxidative degradation caused by light, moisture, heat and some chemicals. This calls for strict and engineered conditions during the manufacturing process [24].

Although there is no certain limit defined for drug amount, generally, it is advised to be around 50 w/w % or below of the entire tablet, preferably 20 w/w % or below. The dose of the indicated drug must be lower than 400mg for insoluble drugs and 60mg for soluble drugs where critical size for easy swallowing and handling is around 8mm [25].

ODTs are currently in progress, but developing ODTs that contain lipophilic active pharmaceutical ingredients is challenging. However, we must find a suitable technology for ODTs to contain lipophiic active pharmaceutical ingredients.

ODTs have some significant limitations and one of the biggest limitations is palatability. The drug delivery systems of ODT is to disintegrate or dissolve, releasing the active ingredients in the buccal cavity, which then encounter the taste buds and thus must be taste-masked to maintain patient compliance.

Other aspects of the drug-related to formulating ODTs are drugs with larger doses are much more difficult to formulate into ODTs than drugs with smaller doses. E.g., antibiotics like ciprofloxacin with adult dose tablets containing about 500 mg of the drug [26].

Patients on medications that act on the autonomic nervous system, including anticholinergics, are not a good candidates for ODT. Likewise, patients with dry eyes or mouth (Sjögren's syndrome) may be due to a decrease in salivary production are not the ideal candidate for ODT [27].

FUTURE PERSPECTIVE ON ODTs

ODTs are an emerging technology that can improve the oral administration of active ingredients with less bioavailability, such as protein-based peptides. The oral delivery of protein therapeutics hasbeen shown to improve efficacy. That kind of product usually degrades rapidly within the gastrointestinal tract by dispersing and dissolving in the saliva, which would be exceptionally promising for delivering high molecular weight protein and peptides[28].

ODT drug delivery system operates on a variety of therapeutic agents, thereby increasing value by creating more commonly used drugs for treating animals or humans. It is possible to develop new quality control methods to determine the technical features of oral dispersing pills.

New technologies containing lipophilic active pharmaceutical ingredients are in progress, but developing formulation technologies for ODTs that comprise lipophilic active pharmaceutical ingredients is a challenge. New ODT technologies should be developed to tackle this challenge [29].

It could be a new development in ODT technology with the development of ODTs with controlled-release features which can deliver drugs with a half-life of as short as 12-24 hours. Those developments' extra comfort and consistency will be widely used [30].

ODTs are already used to deliver a number of different active drugs, but the technology has not yet been adapted for use with a broad range of products. The next generation of ODTs may be able to deliver even more medicines, including those that currently require injection.

CONCLUSION

ODTs have become an integral part of modern pharmacotherapy. Their use has increased in recent years, as they have distinct advantages over other drug delivery technologies, such as the ability to provide therapeutic levels of drug consumption in a fast manner. In the future, ODT manufacturers will be challenged to reduce costs by finding ways to manufacture with conventional equipment, reduce packaging variety, enhance mechanical strength, and increase the ability of the ODT to mask the bad taste. However, the advantages of using ODTs over conventional tablets include improved patient compliance due to noninvasiveness and easy swallowing, more rapid drug release, and enhanced drug absorption. Today, at least two hundred ODT products are available on the market, and some manufacturers add more than one ODT product into their line. Most of these ODT products contain pharmaceutical-grade ODTs, which are usually derived from the same raw materials, have the same manufacturing specifications, are formulated to the same specifications, and are often produced by the same manufacturers. The use of ODTs is expected to extend in the future, as they are being considered as an alternative to parenteral treatments in certain cases, such as those involving the gastrointestinal, central nervous system, and pain systems. In addition, developing more novel ODT formulations will further expand the scope of ODTs as a drug delivery system.

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