Orodispersible Tablets: A Promising Approach Over Conventional Tablets

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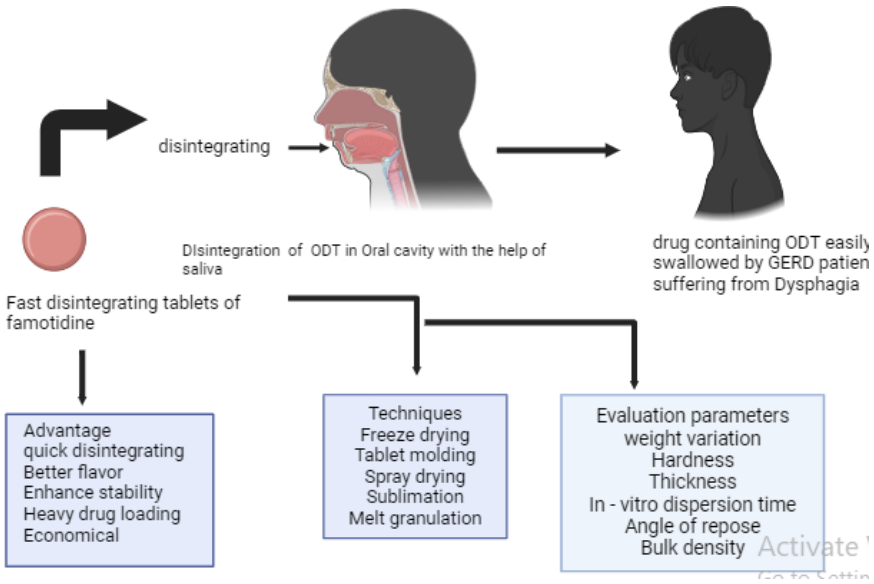
ABSTRACT

Nowadays, the most widely used and practical method of consuming a range of dose forms, such as tablets, capsules, syrups, suspensions, elixirs, etc., is orally. However, some patients, including as bedridden patients and pediatric patients, have trouble swallowing these formulations. Since orodispersible tablets are a novel dose form that dissolves in the mouth in one to three minutes without chewing or the need for water, its primary goal is to increase bioavailability and patient compliance. The article explores the specifics of a number of cutting-edge technologies, including their advantages and disadvantages, including tablet molding, sublimation, freeze drying, direct compression, and rapid dissolving films. Patented technologies like Zydis, Wow Tab, Flash Tab, Oro Quick, and Orosolv have been used by numerous scientists to create orodispersible tablets. These tablets are evaluated using the following methods: Wetting time, water absorption ratio, weight fluctuation, tensile strength, friability, and dissolving test.

Graphical abstract



KEYWORDS: Orodispersible Tablets, Dysphagia, Bioavailability, Natural Superdisintegrant, Patented Technology.

INTRODUCTION:

The most important and useful way to distribute drugs is most likely orodispersible prescription administration.[1]Originally, medication administration methods employed conventional dose formats. Oral medication distribution is the most popular and well-known approach. Oral dose forms are widely used because they are less costly than other dosage forms and easier to use for self-administration.[2]As a result, the pharmaceutical industry started generating solid oral dose forms (SODF) that are easy for patients to take, such as tablets that are dispersible.[3]It is generally acknowledged that oral administration is possible

for as much as 50–60% of all dose types.[4]Swallowing problems are a common issue affecting patients of all ages, although they are particularly prevalent in juvenile and elderly patients because of physiological changes connected to these populations.[5]Before being swallowed, uncoated orodispersible tablets (OTs) disintegrate immediately in the mouth. Tablet swallowing issues may be alleviated by creative and innovative oral pharmaceutical administration techniques that dissolve or disperse immediately in the mouth without the need for water, frequently within a few seconds after application.[6]Without a doubt, the most popular way to deliver medications, both in liquid and solid dosage forms, is orally.[7]Many patients have trouble swallowing tablets, particularly solid gelatin capsules, which can be problematic for both younger and older people. Fast dissolving tablets are a useful tool for solving such issues.[8]The quick disintegration and/or dissolution of these dosage forms upon contact with saliva delivers the medicine, bypassing the requirement for water during administration. This feature is particularly appealing to patients who are younger or older.[9] Manufacturers plainly make more money from oral dosage forms than from parenteral ones, which usually need to be administered by trained staff. The fact that more than 80% of drugs created in the US with the intention of producing systemic effects are sold as oral dosage forms serves as evidence of this. This is because patients can administer oral dosage forms on their own.[10]Other names for oral dissolving tablets (ODTs) include rapidly melting, mouth-dispersing, melt-in-mouth, quick dissolving/disintegrating, and porous.[11-12]ODTs are unit solid dosage forms that offer small packaging, easy manufacture, accurate dosing, good stability, and patient handling.[13]However, these dosage forms were approved as orodispersible tablets by the United States Pharmacopoeia (USP) out of all the criteria described above. The phrase "orodispersible tablet" has been used by the European Pharmacopoeia in recent years to refer to tablets that dissolve easily three minutes prior to ingestion.[14-15]Numerous technological methods, including direct compression, mold-making, and freeze-drying, can be used to create orodispersible tablets. Each technique has benefits and drawbacks.[16]There are several technological methods for producing orodispersible tablets, including mold-making, direct compression, and freeze-drying. All methods have advantages and disadvantages.[17]When using traditional tablets, patients who are bedridden, young patients, and elderly patients frequently experience difficulty swallowing, which can result in low patient compliance.[18]A drug's bioavailability is contingent on its absorption, which is affected by its permeability through the gastrointestinal membrane and its solubility in gastrointestinal fluid.[19]These drugs are available as orodispersible: Ornidazole,[20]Naproxen sodium,[21]Metoclopramide Hydrochloride,[22]Piroxicam,[23]VenlafaxineHydrochloride,[24]Carbimazole,[25]Flutamide,[26]Granise tron Hydrochloride,[27]Orlistat,[28] Ondansetron Hydrochloride.[29]

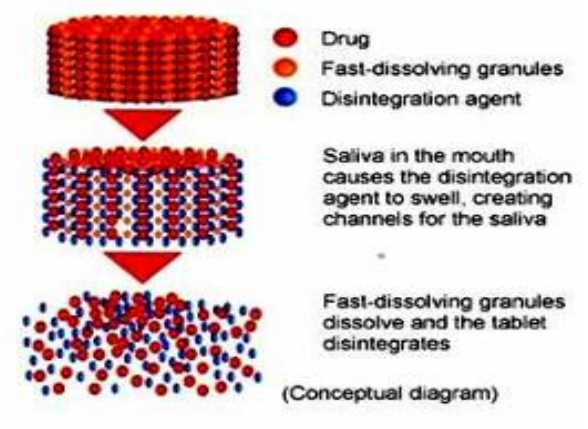


Fig.1: Diagram of the definition of FDTs

SALIENT FEATURE OF ORODISPERSIBLE DRUG DELIVERY SYSTEM:

- Why it is easy to give medicine to patients who don't want to take it, such those in the geriatric, mental, and pediatric categories.
- Accurate dosage and ease of administration in comparison to liquids.
- One very helpful feature is the option to consume the dosage without water for patients who are frequently on the road and may not always have access to it.
- Rapid drug absorption and dissolution, which may provide an immediate commencement of effect. Saliva flowing down into the stomach increases the bioavailability of several medications by absorbing them from the neck and oesophagus.
- With its benefits, the potential to offer a solid form of a liquid medication.
- Pregastric absorption can lead to reduced dosages and fewer adverse effects, which can enhance bioavailability and clinical performance.[30-31]

CRITERIA FOR ORODISPERSIBLE TABLET

- Although the pills should melt or dissolve in the tongue in a few seconds, it should be possible to take them without water. It combines flavor concealment with success.
- Have the freedom to walk about without fear of breaking.
- It feels good to eat.
- During delivery via oral route, the amount of trace in the mouth should be minimal to nonexistent.
- React minimally to changes in humidity and temperature.
- Permit the tablet to be produced at a minimal cost using common processing and packaging equipment.[32]

ADVANTAGES OF ORODISPERSIBLE TABLETS

Quick disintegration technology states:

- Water is not required.
- Chewing is not required.
- Better flavor.
- Enhanced stability.
- Perfect for active ingredients with controlled or prolonged release.
- Enables the loading of strong drugs.
- The ability to combine the advantages of liquid medication with solid preparation.
- Excellent for patients who struggle to swallow medications and have oesophageal reflux disease.
- Possess a pleasing mouthfeel and a taste that is adequate.
- After oral delivery, leave the least amount of residue in the mouth.
- Ensure quick response times when desired.
- Pleasantly textured mouth.
- Economical.[33-34]

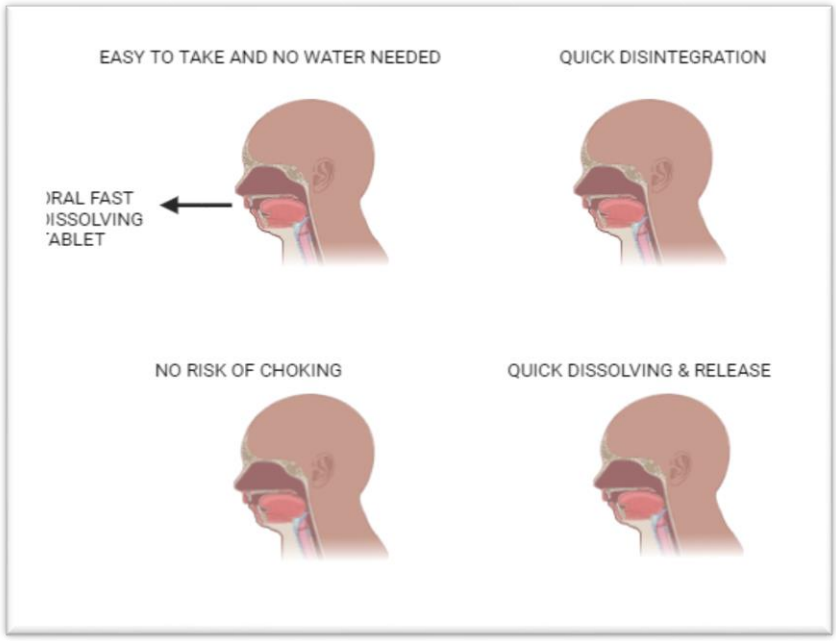


Fig.2: Advantages of fast dissolving tablet

LIMITATIONS OF ORODISPERSIBLE TABLETS

FDTs are extremely permeable soft molded measurements that can fit into a tablet with minimal compression.

- Compression causes tablets to become fragile and challenging to hold. Since it is challenging to make drugs with unpleasant tastes as FDT, more security precautions need to be taken.
- Before making this kind of medication, it must be ingested. As a result, in a normal scenario, certain FDT cannot maintain their physical reliability.

- Moisture-related ailments need a customized treatment plan. Dry mouth from decreased salivary flow might not work well with certain pill formulations.
- The medicine and dosage form are immobile.
- The total bioavailability and the rate of absorption from the saliva solution.
- Grittiness or overpowering taste on the tongue could be the result of a poorly formulated pill. [35- 37]

CHALLENGES IN FORMULATION ORODISPERSIBLE TABLETS

1. Palatability:

Since most oral disintegrating drug delivery strategies break down or disintegrate in the patient's mouth, releasing the active compounds that reach the taste buds, it is necessary to mask the taste of the medications in order to ensure patient compliance.

2. Mechanical strength:

Usually, FDTs decompose in under a minute. One of the most difficult tasks to complete while keeping a high level of mechanical strength is this one. There is a significant risk that one of these tablets will shatter during patient treatment, packaging, or shipping because many FDTs are brittle. Zydis-based tablet technologies require specific packaging. The idea that a higher mechanical strength will lead to a slower rate of disintegration seems logical. Therefore, finding the right balance between these two factors is always essential.[39]

3. Hygroscopicity:

Many oral dissolving dosage forms are hygroscopic, which means that at typical humidity and temperature levels, they lose their physical integrity. Because of this, they need to be protected from moisture, which calls for the adoption of particular product packaging.[40-41]

4. Amount of drug:

The quantity of medicine required in each unit dose is one possible barrier to the establishment of ODTs. The lyophilization procedure should use no more than 60 mg of soluble medications and 400 mg of insoluble components.[42]

5. Size of tablet:

It was shown that tablets between 7 and 8 mm are the easiest to swallow, whereas tablets larger than 8 mm are the easiest to handle. It is really challenging to create a tablet that is both portable and controllable.[43]

6. Good packaging design:

The packaging design should be taken into consideration early in the development stages in order to safeguard ODTs from moisture and other environmental dangers.[44]

DISADVANTAGES OF ORODISPERSIBLE TABLETS:

- Because orodispersible pills are hygroscopic, they need to be kept in a dry environment.
- ODT needs specific packaging to guarantee the steady product's stability and safety.
- The tablets' mechanical strength is frequently insufficient. Therefore, handling must be done carefully.
- Inadequate tablet manufacturing may result in an unpleasant flavor and a grainy mouthfeel.
- To ensure the stability and security of the stable product, ODT requires specialized packaging.
- Inappropriately formed tablets may taste terrible and leave the tongue feeling scratchy.[45-47]

EXCIPIENTS USED IN THE FORMULATION OF ORODISPERSIBLE TABLETS:

The formulation of the fast-dissolving tablet requires specific excipients.

Superdisintegrants: The presence of superdisintegrants, which dissolve under direct compression, is the most important factor influencing the rate of disintegration. Disintegration is accelerated even more by using extra formulation elements such effervescent agents and water-soluble excipients.[48- 50]

These are two types superdisintegrants are used such as –

a) Natural Superdisintegrants: These superdisintegrants are safe and tasteless, and they come from natural sources. Natural materials such soy polysaccharide, Chitosan, guar gums, agar, and Isapghula husk mucilage (Plant ago ovate) are utilized as superdisintegrants.
b) Synthetic Superdisintegrants: These superdisintegrants encompass crospovidone, sodium starch glycolate, and sodium croscarmellose.

Emulsifying agents: These ingredients eliminate the need for chewing, swallowing, or drinking water by rapidly dissolving and releasing the drug. Their inclusion can range from 0.05% to 15% of the final mixture's weight. Emulsifying compounds such as lecithin, propylene glycol esters, and sucrose esters are employed.

Flavoring & Sweetening Agents: These ingredients help patients find the orodispersible tablets more edible and agreeable, and sweeteners enhance the formulation's pleasant flavor. Some examples of sweeteners are dextrose, sugar, fructose, and sodium saccharine.

Bulking Substances: The bulkiness property of the formulation, texture, and dissolve time in the mouth are all much improved by these compounds. Mannitol, lactose derivatives, sorbitol, fructose, and others were among the agents.

Table 1.1: List of Superdisintegrants[51]

Superdisintegrants	**Example**	**Mechanism of Action**	**Special comment**
Crosscarmellose® Ac-Di-Sol® Nymce ZSX® PrimelloseRSolutab® Vivasol® L-HPC	Cross-linked Cellulose	-Swells 4-8 folds in < 10 seconds. -Swelling and wicking Both.	-Swells in two dimensions. -Direct compression or granulation -Starch free
Crosspovidone Crosspovidon M® Kollidon® Polyplasdone	Crosslinked PVP	-Swells very little and returns to original size after compression but act by capillary action	-Water insoluble and spongy in nature so get porous tablet
Sodium starch glycolate Explotab® Primogel®	Crosslinked Starch	-Swells 7-12 folds in < 30 seconds	-Swells in three dimensions and high level serve as sustain release matrix
Soy Polysaccharides Emcosoy	Natural super disintegrant		-Does not contain any starch or Sugar. Used in Nutritional products.
Calcium silicate		-Wicking action	Highly porous, Optimum concentration is between 20-40%

TECHNIQUE USED IN PREPARATION OF ORODISPERSIBLE TABLETS:

1. Direct Compression:

The easiest and least expensive way to make tablets is by direct compression. ODT can now be manufactured using this process because to improved excipients, particularly sugar-based excipients and superdisintegrants.

2. Melt granulation

A meltable binder serves in the process of "melt granulation technique," which effectively agglomerates pharmaceutical powders. The fact that this approach doesn't require water or organic solvents is a definite benefit over conventional granulation. Since there is no drying process involved, this method requires less time and energy than wet granulation. This method aids in the rapid disintegration of medications that are poorly soluble in water, such as griseofulvin.[52]

3. Sublimation

This technique depends on the tablet's composition, which includes inert volatile compounds including ammonium bicarbonate, camphor, and urea.[53]Following manufacturing; the volatile chemical is sublimated in a vacuum by lower pressure and temperature, leaving the tablets porous. Fast Disintegration isn't always the case with typical sorts. Use volatile solvents including cyclohexane or benzene to enhance the porous structure's dissolution.[54]

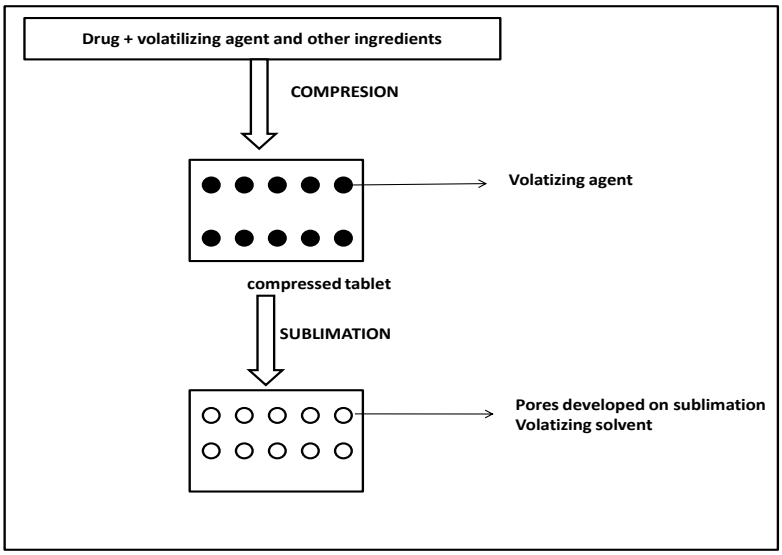


Fig.3: Schematic diagram of sublimation techniques for preparing orodispersible tablets

4. Mass-Extrusion

The active blend is relaxed by the solvent mixture of methanol and water-soluble polyethylene glycol. An extruder or syringe releases the softened bulk into uniform segments, which are then heated to form tablets. Additionally, the bitterness from the dried cylinder can be used to mask the flavor of medicine grains.[55]

5. Spray Drying

As the processing solvent evaporates during step 11, the approach yields extremely porous and tiny bits. During the MDT manufacturing method, hydrolyzed and nonhydrolyzed gelatin served as the supporting matrix, sodium starch glycolate or crosscarmellose sodium as a superdisintegrant, and mannitol as a bulking agent. The rate of breakdown and disintegration was accelerated by the addition of alkali substances like sodium bicarbonate or acidic

chemicals like citric acid. With this formulation approach, the powder is porous and dissolves in less than 20 seconds.[56]

6. Tablet Modling

Solid dispersions are the tablets made with this technique. The drug's physical form in the tablets is determined by its degree of dissolution in the wetted material. The medicine may be present in the matrix as distinct particles or as tiny particles. It may partially dissolve in the molten carrier, leaving behind residue scattered throughout the matrix, or it may dissolve entirely to produce a solid solution. The mouth feel, drug dissolve rate, and disintegration time will all be impacted by the type of dispersion.[57]

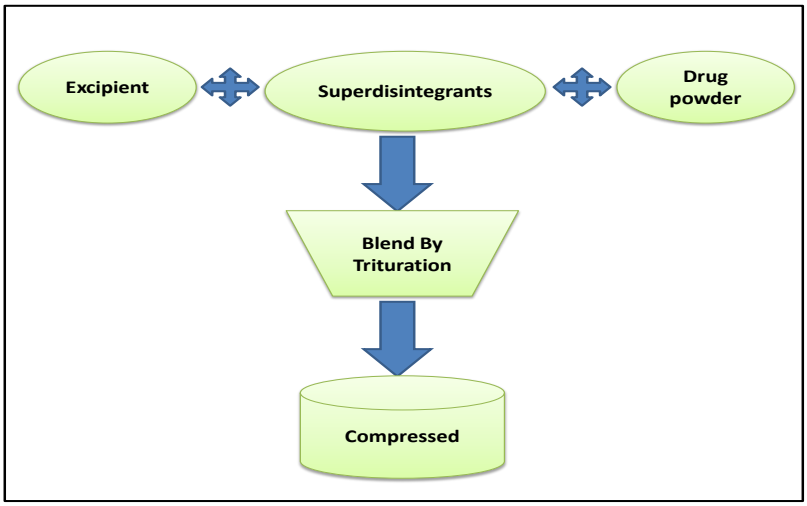


Fig.4: Schematic diagram of sublimation techniques for preparing orodispersible tablets

7. Nanoionization

The drug's particles are crushed using a special wet-milling method to reduce them to nanosize for the nanoionization procedure. Prior to being crushed into FDT, the drug's nanocrystals must be surface-adsorption stabilized on certain buffers to prevent agglomeration.[58]

PATENTED TECHNOLOGIES FOR ORODISPERSIBLE DRUG DELIVERY SYSTEM

1. Zydis

Tablets with freeze-dried active ingredients that dissolve quickly in the tongue make up the drug delivery method. Lyophilizing a medication suspension or solution including a range of excipients, including polymers, polysaccharides, preservatives, pH adjusters, flavors, sweeteners, and colors, and then sealing it into blisters is how freeze-dried tablets are made. After being packaged and shipped, the blisters go through an interior freeze-drying process.[59]

2. Orasolv technology

Another patented creation is Orasolv. Because Orasolv tablets are somewhat compressed, they are crumbly and less powerful than regular tablets. For Orasolv, CIMA LABS creates customized handling and packaging systems. The minimum degree of compression has the benefit of not affecting the taste masking particle coating due to splitting during pressing.[60]

3. Flashtab Technology

The patent holder for the Flashtab technology is Prographarm Laboratories. Microcrystals are the material that functions in the tablets produced using this technique. To make medication microgranules, standard methods including coacervation, micro encapsulation, and extrusion spheronization can be employed. Conventional tabletting technology was utilized in each processing stage.[61]

Table 1.3: Commercially available ODT products[62]

Brand name	Active ingredient	Manufacturer
Rofaday MT	Rofecoxib	Lupin
Benadryl fast melt	Diphenhydramine	Warner Lambert
Domray MD	Domperidone	Ray Remedies
Orthoref MD	Rofecoxib	Biochem
Zelapar TM	Selegi Nlline	Amarin Corp
Kemstro	Baclofen	Schwarz Pharma
Febrecto	Paracetamol	Prographarm
Imodium instant melts	Loperamide HCL	Janseen
Values	Valdecoxib	Glenmark
Pepcid ODT	Famotidine	Merek
Claritin Reditabs	Loratidine	Schering-Plough
Mosid MT	Mosapride	Torrent

EVALUATION PARAMETERS OF ORODISPERSIBLE TABLET

- **Pre Compression Parameters of Tablets:** [63-66]

1. Angle of Repose:

The fixed funnel method was used for determining the angle of repose. A vertically adjustable funnel was used to pour the mixture until the maximum cone height (h) reached the desired level.

Using the formula (Rockville et al., 2007), where r is the pile's radius, h is its height, and r is its angle of repose, the angle of repose was determined after the heap's radius (r) was measured. = -1.

2. Bulk Density:
A chemical's bulk density can be substantially influenced by how it is crushed, crystallized, or produced. Using a large funnel, the presieved mixture was dumped into a graduated cylinder, and the weight and volume were recorded in order to determine the bulk density.

3. Tapped Density:
To measure the taped density, mechanical tapper equipment and a graduated cylinder containing a predefined volume of mix were utilized. This continued until the volume of the powder bed decreased to a minimum after a predetermined number of taps. Make use of the cylinder's weight and small capacity. The following formula was used to arrive at the tapped density: The "tapped density" can be estimated by dividing the weight of the mix by the tapped volume.

4. Carr's Index:
Carr's index has been determined using both bulk density and tapped density readings. The Carr's index was computed using the following formula.

Carr's index= (tapped density- bulk density)/tapped density × 100

5. Hausner's ratio:
It shows the tapped density relative to the bulk density of the powder or mix and the flow properties of the powder.

Hausner's ratio= tapped density/ bulk density

- **Post compression parameters:**

1. Hardness:
A tablet's hardness is measured by the force required to shatter it over its whole circumference. The tablets' hardness was evaluated using diametral compression and a Monsanto Hardness Tester.[67]

2. Thickness:
Tablet thickness plays an integral part in both counting with filling equipment and replicating appearance. The tablets' constant thickness is used by some filling equipment as a counting mechanism. The vernier caliper was used to record the thickness.[68]

3. Weight variation:
The average weight of twenty randomly chosen pills was calculated. Each tablet was then weighed independently, and the weights were contrasted with the mean.[69]

4. Friability:
The friability of tablets is determined by their mechanical strength. Friability has a limit bound of 0.1 to 0.9. The friability is tested using the Roche friabilator. The friabilator is filled

with a pre-weighed pill. For four minutes, the friabilator rotates the tablets 100 times at 25 rpm. The weight loss, which is a gauge of friability and is given as a percentage as follows, is determined by reweighing the tablets at the end of the test.[70]

% Friability = Loss in weight X 100 Initial weight.

5. Disintegration time:
Using the tools listed in I.P.-1996, six tablets were examined. The disintegration medium was 37°C ± 2°C distilled water. The amount of time it took for the pill to dissolve entirely and remove any seductive ingredients from the apparatus was noted.[71]

6. In-vitro dispersion time:
In order to test the in vitro dispersion time, 50 milliliters of PH 6.8 Sorenson's buffer were added to a beaker containing a tablet. Three tablets were chosen at random from each formulation, and then an in vitro dispersion time test occurred.[72]

7. Wetting time:
A tablet containing six milliliters of pH 6.8 phosphate buffer was held in place by a small Petridish (ID = 9 cm) on a double-folded 12 cm × 10.75 cm piece of tissue paper. The length of time it took for the paper to soak completely was noted. The average wetting time was recorded following the random selection of three tablets from each formulation.[73]

8. Dissolution Study:
In vitro drug release testing has been conducted using the paddle-type USP dissolving equipment II at 50 rpm in 900 ml of phosphate buffer (pH 6.8) at 37±0.5ºC. Ten milliliters of the material are extracted and filtered at various points in time. After every withdrawal, the same amount of medium is injected in order to keep the tank full. The UV Spectrophotometer is used to measure the materials' absorbance at a predetermined maximum. The typical amounts of drug released are displayed by charting the cumulative fraction of drug release against time.[74]

9. Accelerated stability studies:
The quick dissolving tablets were stored during the accelerated research at RH 75% ± 5%, (i) 40 ± 1°C, (ii) 50 ± 1°C, and (iii) 37 ± 1°C in compliance with ICH recommendations. After fifteen days, the tablets were removed and inspected for physical defects, including fractures, dissolution, hardness, and disintegrations. To ascertain the degradation kinetics, the resulting data is subsequently fitted into first-order equations.[75]

CONCLUSION

In comparison to normal solid oral dose forms (SDF), ODTs may be more effective since the Drug Delivery System (DDS) helps address some of the problems with SDF, such as the incapacity of old and young patients to chew tablets. This drug delivery mechanism is among the new DDS's greatest breakthroughs. Improved bioavailability, rapid onset of action, user-

friendliness, and patient compliance are just a few advantages that ODTs provides. Because ODTs function quickly (within a minute), they might be the most widely used and approved dose form in the future. Their unique benefits, like the ability to administer them anywhere, at any time, and without water, result in higher patient compliance in the busy world of today. The majority of pharmaceutical companies manufacture a variety of formulations in ODT forms due to the numerous advantages of ODTs. The popularity of these dose forms will undoubtedly grow in the future due to rising patient demand.

REFFERENCES

1. D. B. Patel, K. J. Patel, P. D. Bharadia. Formulation and evaluation of orodispersible tablet of ivabradine hydrochloride. Pharmaceutical and biological evaluations. June 2017; vol.4 (issue3):162-170.issn2394-0859. **DOI:10.26510/2394-0859.pbe.2017.25.**

2. Kushagra Khanna, Gauravi Xavier, Suresh Kumar Joshi, Aashish Patel, Sakshum Khanna, Vipin and Bhawna Goel. Fast Dissolving Tablets- A Novel Approach. International Journal of Pharmaceutical Research & Allied Sciences, 2016, 5(2):311-322. ISSN : 2277-3657.

3. Sonia Iurian, Ioan Tomuță, Sorin E. Leucuța. Formulation of Orodispersible Tablets Containing Meloxicam and their in Vitro and in Vivo Characterization. Farmacia, 2014, Vol. 62, 6.

4. Gopal S. Gandh, Dharmendra R. Mundhada, Shyamala Bhaskaran. Formulation and Evaluation of Orodispersible Antacid Tablet for Geriatric Patient. Journal of Pharmaceutical Research and Opininion.

5. Jashanjit Singh and Rajmeet Singh. Optimization and Formulation of Orodispersible Tablets of Meloxicam. Tropical Journal of Pharmaceutical Research, April 2009; 8 (2): 153-159. https://doi.org/10.4314/tjpr.v8i2.44524.

6. V.P. Pandey and J.Joysa Ruby. Orodispersible Tablets – A Review. World Journal of Pharmacy and Pharmaceutical Sciences. Volume 3, Issue 9, 129-135. ISSN 2278 – 4357.

7. Kamlesh Wadher, Kunal Dhote, Monika Mane, Ajit Khapne, Anjali Gaidhane Milind Umekar. Orodispersible Dosage Form: Advancement and Challenges. International Journal of Pharma Research and Health Sciences 2019; 7 (4): 3013-3019. ISSN: 2348-6465. DOI: 10.21276/ijprhs.2019.04.01.

8. Raghavendra Rao n.g , Ravi Kumar Kota , Setty c.m , Purushotham Rao. K .Formulation and Evaluation of Fast Dissolving Chlorthalidone Tablets. International Journal of Pharmacy and Pharmaceutical Sciences, Vol. 1, Suppl 1, Nov.-Dec. 2009.

9. Dali SHUKLA, Subhashis CHAKRABORTY, Sanjay SINGH, Brahmeshwar MISHRA. Mouth Dissolving Tablets I: An Overview of Formulation Technology. Sci Pharmaceutica. https://doi.org/10.3797/scipharm.0811-09-01.

10 .Rafah Khames Mahal. Dr.Laith H. Samein. Dr. Muyad A. Shehab. Formulation and In-Vitro Evaluation of Orodispersible Tablet. Rafah Khames Mahal. International Journal of Pharma Sciences and Research (IJPSR).

11. Dalapathi Gugulothu, Preshita Desai, Pranav Pandharipande, and Vandana Patravale. Freeze drying: exploring potential in development of orodispersible tablets of sumatriptan succinate. 2014 Informa Healthcare USA, Inc.. ISSN: 0363-9045 (print). DOI:10.3109/03639045.2013.871551.

12. M. Swamivelmanickam, R. Manavalan and K. Valliappan. Mouth Dissolving Tablets: An Overview. International Journal of Pharmaceutical Sciences and Research, 2010; Vol. 1 (12): 43-55. ISSN: 0975-8232.

13. Johnny Edward Aguilar, Encarna García Montoya, Pilar Pérez Lozano, Josep M. Suñe Negre, Montserrat Miñarro Carmona and José Ramón Ticó Grau,. New SeDeM-ODT expert system: an expert system for formulation of orodispersible tablets obtained by direct compression. Formulation tools for pharmaceutical development.

14. P. V. Swamy, S. N. Gada, S. B. Shirsand, M. B. Kinagi and H. Shilpa. Design and Evaluation of Cost Effective Orodispersible Tablets of Diethylcarbamazine Citrate by Effervescent Method. P.V.Swamy et. al. / International Journal of Pharma Sciences and Research (IJPSR) Vol.1(6), 2010, 258-264. ISSN : 0975-9492.

15. Kiran, Dhakane, Minal Rajebahadur , Pradip Gorde., Pawan Salve. Fast Dissolving Tablet: A Future Prospective. Kiran, Dhakane et al. / Journal of Pharmacy Research 2011,4(11),4176-4180. ISSN: 0974-6943.

16. L . Segale, L. Maggi, E. Ochoa Machiste, S. Conti , U. Cont , A. Grenier , C. Besse. Formulation Design and Development to Produce Orodispersible Tablets by Direct Compression. J. Drug del. Sci. Tech., 17 (3) 199-203 2007.

17. S Furtado, R Deveswaran, S Bharath, BV Basavaraj, S Abraham and V Madhavan. Development and Characterization of Orodispersible Tablets of Famotidine Containing a Subliming Agent. Tropical Journal of Pharmaceutical Research, December 2008; 7 (4): 1185-1189.

18. Karan Malik , Gurpreet Arora , Inderbir Singh. Locust bean Gum as Superdisintegrant – Formulation and Evaluation of Nimesulide Orodispersible Tablets. Karan Malik et al.

19. J.Preethi, MD Farhana, B.Chelli Babu, MD.Faizulla, Debjit Bhowmik , S.Duraivel. Recent Trends of Polymer Usage in the Formulation of Orodispersible Tablets. Indian Journal of Research in Pharmacy and Biotechnology. Volume 1(2). ISSN: 2320 – 3471(Online).

20. Kulkarni Maushumi S, Zeeshan Ahmed, Bhise Kiran S., Somwanshi shekhar V. Formulation and Evaluation of Orodispersible Tblet of Ornidazole. International Journal of Pharmaceutical Studies and Research.Vol. I/ Issue II/October-December, 2010/39-47.

21. Neha Vishal Gandhi,S. S. Khadabadi, S. S. Angadi . Formulation and Evaluation of Orodispersible Tablet of Naproxen Sodium. International journal of Pharmaceutical Sciences and Research 2011.Vol. 2, Issue 11. ISSN: 0975-8232.

22. Jayashri G. Mahore , Kamlesh J. Wadher , Milind J. Umekar. Formulation and in vitro Evaluation of Taste Masked Orodispersible Tablet of Metoclopramide Hydrochloride. International Journal of Pharmtech Research. Vol.2, No.3, pp 1827-1835, ISSN : 0974-4304.

23. N. Ravi Kiran, S. Palanichamy, M. Rajesh, T. Godwin Rajadhas, V. Anusha, N. Parasakthi and A. Thanga Thirupathi. Formulation and Evaluation of Orodispersible Piroxicam Tablets. Jounral of Pharmaceutical Sciences and Research. Vol.2 (10), 2010,615-621. ISSN:0975-1459.

24. B. Senthilnathan and Anusha Rupenagunta. Formulation Development and Evaluation of Venlafaxine Hydrochloride Orodispersible Tablets. International journal of pharmaceutical sciences and research (2011), Vol. 2, Issue 4. ISSN: 0975-8232.

25. Mohammed Iqdam al-Shadeedi, laith h. Samein, Muayad a. Shehab. Formulation and Evaluation of Carbimazole Orodispersible Tablet. International Journal of Pharmacy and Pharmaceutical Sciences. Vol 5, Suppl 1, 2013. ISSN- 0975-1491.

26. Kadria A. Elkhodairy , Maha A. Hassan , Samar A. Afifi . Formulation and Optimization of Orodispersible Tablets of Futamide. Sudi Pharmaceutical Journal.

27. Chinmaya Keshari Sahoo, Nalini Kanta Sahoo , Madhusmita Sahu , Alok kumar Moharana , Deepak Kumar Sarangi. Formulation and Evaluation of Orodispersible Tablets of Granisetron Hydrochloride Using Agar as Natural Super disintegrants. Pharmaceutical Methods, Vol 7, Issue 1, Jan-Jun, 2016.

28 .Kambham venkateswarlu, S. B. Thirumalesh Naik, K. B. Chandrasekhar. Formulation and in Vitro Evaluation of Orlistat Orodispersible Tablets for Enhancement of Dissolution Rate. International Journal of Pharmacy and Pharmaceutical Sciences. Vol 8, Issue 4, 2016. ISSN- 0975-1491.

29. Avani R. Gosai, Sanjay B. Patil and Krutika K. Sawant. Formulation and Evaluation of Oro Dispersible Tablets of Ondansetron Hydrochloride by Direct Compression using Superdisintegrants. International Journal of Pharmaceutical Sciences and Nanotechnology Volume 1,Issue 1, April - June 2008.

30. Bhupendra G Prajapati and Nayan Ratnakar. A Review on Recent patents on Fast Dissolving Drug Delivery System. International Journal of Pharm Tech Research. ISSN : 0974-4304 Vol.1, No.3, pp 790-798.

31. Bhomik D, Krishnkanth CB, Pankaj and Chandira RM, "Fast dissolving tablet: an overview." Journal of Chemical and Pharmaceutical Research. 2009, 1(1), 163- 177. 6.

32 .Sudarshan B. Aher , Kajal S. Gahide. FAST DISSOLVING TABLETS: REVIEW. INDO AMERICAN JOURNAL OF PHARMACEUTICAL SCIENCES. Volume2 (4), 815-826. ISSN 2349-7750.

33. N.S. Ganesh. Orodispersible Tablets: An Overview of Formulation and Technology International Journal of Pharma and Bio Sciences.

34. Amol Patil, Dhanesh H. Sali, SatishS. Reddi, NikhilS. Wargade, Santosh K. Mohapatra, Bharat V. Paygude· Recent Trends and Formulation Technology of Orodispersible Tablets.

35. Ganesh Ghale, Krishna Shimge, Vikram Saruk and Shraddha Pattewar. Fast Dissolving Tablets. World Journal of Pharmaceutical Research. Volume 7, Issue 16, 427-438. ISSN 2277– 7105.

36 .Ravi, Geeta Rajput, Amit Kumar. A Review Article on Orodispersible tablet Formulation. The pharma innovation – journal. Vol. 2 No. 2 2013. ISSN: 2277- 7695.

37. Ajoy Bera and Ashish Mukherjee. A Detailed Study of Mouth Dissolving Drug Delivery System. Acta Chim and pharmaceutica indica Acta Chim. Pharm. Indica: 3(1), 2013, 65-93 ISSN 2277-288X.

38 .Md.Nehal Siddiqui, Garima Garg, Pramod Kumar Sharma. Fast Dissolving Tablets: Preparation, Characterization and Evaluation: An Overview. International Journal of Pharmaceutical Sciences Review and Research. Volume 4, Issue 2, September – October 2010; Article 015. Volume 4, Issue 2, September – October 2010; Article 015.

39. Sehgal Prateek , Gupta Ramdayal , Singh Umesh Kumar , Chaturvedi Ashwani , Gulati Ashwini , Sharma Mansi. Fast Dissolving Tablets: A New Venture in Drug Delivery. Fast Dissolving Tablets: A New Venture in Drug Delivery. ISSN: 2249-3387.

40. Jaysukh J Hirani, Dhaval A Rathod , Kantilal R Vadalia. Orally Disintegrating Tablets: A Review. Tropical Journal of Pharmaceutical Research, April 2009; 8 (2): 161-172.

41. Pankaj Sharma, Raneev Thakur and Priyanka Nagu. Fast Disintegrating Tablets: A Review. European Journal of Biomedical AND Pharmaceutical sciences. Volume 5, Issue 9, 169-180.

42. Vinita Chaurasia, Vikas Kumar , Brajesh K Tiwari , Aakancha Jain , Dharmendra Jain. Orodispersible Tablets: An Overview of Technology. International Journal of Advanced Research and Review, 1(6), 2016; 156-172.

43. Punya Prakash, Shetty Nireeksha Vijay, Vishwakarma Mukesh, Krishnananda Kamath Kunjal and A. R. Shabaraya. A review of Fast Dissolving Tablets. World Journal of Pharmaceutical Research. World Journal of Pharmaceutical Research. Volume 12, Issue 3, 131-142. ISSN 2277– 7105

44. Anupam Roy. Orodispersible Tablets: A Review. Asian Journal of Pharmaceutical and Clinical Research. Vol 9, Issue 1, 2016. ISSN - 0974-2441.

45. Raj Kumari, Chandel Priya, Kapoor Ankita. Fast dissolving tablets: needs to enhance bioavailability. International research journal of pharmacy. Issn 2230 – 8407. Doi: 10.7897/2230-8407.04512.

46. Nikita K. Patel, Sahilhusen I. Jethara, Mukesh. S. Patel. A Review on Orodispersible Tablets – As a Novel Formulation for Oral Drug Delivery Systems. Journal of pharmaceutical science and boiscientific research. JPSBR: Volume 5, Issue 3: 2015 (286-294). ISSN NO. 2271-3681.

47. Mukesh Chandra Sharma and Monika Leel. A Review: Oral Dispersible Tablets. International Journal of Drug Development and Research. Vol.14 No.1:171. ISSN 0975-9344.

48. Sudarshan B. Aher , Kajal S. Gahide. FAST DISSOLVING TABLETS: REVIEW. INDO AMERICAN JOURNAL OF PHARMACEUTICAL SCIENCES. Volume2 (4), 815-826. ISSN 2349-7750.

49. Nitin K Kapse, Vilas P Bharti, Arunadevi S Birajdar, Anirudha V Munde, Pranita P Panchal. Co-Processed Superdisintegrants: Novel Technique for Design Orodispersible Tablets. Co-Processed Superdisintegrants: Novel Technique for Design Orodispersible Tablets. ISSN: 2349-2759.

50. Hirani J, Rathod DA and Vadalia KR, "Orally Disintegrating Tablets: A Review." Tropical Journal of Pharmaceutical Research. 2009 April, 8(2), 161-172.

51. Chiman Beri, Isha Sacher. Development of Fast Disintegration Tablets As Oral Drug Delivery System-A Review. Indian J. Pharm. Biol. Res Vol. 1 (3), Sep., 2013 ISSN:2320-9267.

52. Ashish Masih, Amar Kumar, Shivam Singh, Ajay Kumar Tiwari. Fast dissolving tablets: A Review. International Journal of Current Pharmaceutical Research. International Journal of Current Pharmaceutical Research. Vol 9, Issue 2, 2017. DOI: https://doi.org/10.22159/ijcpr.2017v9i2.17382.

53. Ludmila Alvim Pinho; Ana Claudia Temer; Caroline Ribeiro; Livia Lira SÁ-Barreto; Marcilio Sergio Soares Cunha-Filho. The popularization of orodispersible tablets in the pharmaceutical market. in Infarma - Ciências Farmacêuticas · July 2018. DOI: 10.14450/2318-9312.v30.e2.a2018.pp77-84.

54. Nizar A. Jassem. orodispersible Tablets: A Review on Recent Trends in Drug Delivery. in International Journal of Drug Delivery Technology · March 2022.

55. Tanmoy Ghosh, Amitava Ghosh and Devi Prasad. A review on New Generation Orodispersible Tablets and its Future Prospective. International Journal of Pharmacy and Pharmaceutical Sciences. Vol 3, Issue 1, 2011. ISSN- 0975-1491.

56. Alok Kumar Gupta, Anuj Mittal and Prof. K. K. Jha. Fast Dissolving Tablet- A Review. The Pharma Innovation. Vol. 1 No. 1 2012.

57. Sharad A More, Dr. S. K. Mohite. Orodispersible Tablet- A Novel Drug Delivery System. Sharad A More et al / Journal of Pharmaceutical Science and Technology Vol. 4 (1), 2012, 798 -806.

58. Shehla Khan, Sadhana Shahi, Santosh Borde and Saliya Shaikh. Fast Dissolving Tablets: A Novel Drug Delivery System. European Journal of Pharmaceutical and Medical Research. 2017, 4(12), 161-172.

59. Sagar T Malsane , Smita S Aher , R B Saudagar. A Review on Fast Dissolving Tablet. International Journal of Current Pharmaceutical Review and Research; 8(3); 284-292. ISSN: 0976 822X. doi: 10.25258/ijcprr.v8i03.9218.

60. Malode A.J. Rode P.A.. Mouth Dissolving Tablets: An Overview. Ind. J. Res. Methods Pharm. Sci. 2022; 1(6):12-26 ISSN (Online): 2583-3804.

61. Deepika Jain , Mishra Amul. A Review - Formulation & Development of Orodispersible Tablet. International Journal of Pharmaceutical Erudition. ISSN 2249-3875.

62. Amol V. Patil, Dhanesh H. Sali1 , Satish S. Reddi1 , Nikhil S. Wargade1 , Santosh K. Mohapatra1 ,Bharat V. Paygude1. Recent trends and formulation technology of orodispersible tablets. Journal of Pharmacy Research Vol.4.Issue 3. March 2011.

63. Sachin Gholve, Amar Kaware , Sanjay Thonte , Dattahari Kaudewar and Omprakash Bhusnure. ORODISPERSIBLE TABLETS: A SYSTEMATIC REVIEW. World Journal of Pharmaceutical Research. Vol 7, Issue 6, 2018

64. Rasheed SH, Arief M, Gajavalli SR and Hussain SS, "A Comparison of different superdisintegrants in designing of fast dissolving tablets of salbutamol sulphate." Research Journal of Pharmaceutical, Biological and Chemical Sciences. 2011, 2(2), 155- 163.

65. Mohd. Salman Ahmed; Nikita Upadhyay; P.K Dubey. A REVIEW ON FAST DISSOLVING TABLET. Mohd. Salman Ahmed et al, International Journal of Pharmaceutical Sciences & Medicine (IJPSM), Vol.7 Issue. 5, May- 2022, pg. 37-47. ISSN: 2519-9889.

66. R.B. Nawale and K.P. Mohite. Formulation and Evaluation of Domperidone Orodispersible Tablet. International Journal of Pharmaceutical Sciences and Research. Vol. 4, Issue 9.

67. R.B. Nawale and K.P. Mohite. Formulation and Evaluation of Domperidone Orodispersible Tablet. International Journal of Pharmaceutical Sciences and Research. Vol. 4, Issue 9.

68. Pooja Arora, Vandana Arora Sethi. Orodispersible Tablets: A Comprehensive Review. International Journal of Research and Development in Pharmacy and Life Sciences. February - March, 2013, Vol. 2, No.2, pp 270-284. ISSN: 2278-0238.

69. Amol Lende, Dharmendra Mundhada, Rajesh Mujoriya. Formulation Development and Evaluation of Mouth Dissolving Tablet of Anti-allergic Drug (Astemizole). **Asian Journal of Pharmacy and Technology.**

70 .Mayuri R Patil, Nayan A Gujarathi, Bhushan R Rane. Formulation and Evaluation of Mouth Dissolving Tablet: Review Article. Pharma Science Monitor An International Journal of Pharmaceutical Sciences.

71. Maddukuri Sravya, Rajamanickam Deveswaran, Srinivasan Bharath, Basappa Veerbadraiah Basavaraj, and Varadharajan Madhavan. Development of Orodispersible Tablets of Candesartan Cilexetil-β-cyclodextrin Complex. Journal of Pharmaceutics. Volume 2013, Article ID 583536, 13 pages. doi: 10.1155/2013/583536.

72. Rajesh Roshan Rai, Pavithra Chirra, Venkataramudu Thanda. Fast Dissolving Tablets: A Novel Approch to Drug Delivery – A Review. International Journal of Preclinical and Pharmaceutical Research. Vol 3 | Issue 1 | 2012 | 23-32. e - ISSN – 2249-7552.

73. Jyoti Saxena, Digvijay Singh , Amrita Bisht, Arvind Negi , Aman Verma. A Review on Fast Dissolving Tablets. Journal of Medical P'ceutical and Allied Sciences, V 10-I 1, 1004. January-February 2021, P-2658-2663. DOI: 10.22270/jmpas.V10I1.1004. ISSN NO. 2320–7418.

74. Kamal Saroha, Navneet Syan and Ajay Kumar, "Mouth dissolving tablets: An overview on future compaction in oral formulation technologies." Der Pharmacia Sinica. 2010, 1(1), 179-187.

75. Shehla Khan, Sadhana Shahi, Santosh Borde and Saliya Shaikh. FAST DISSOLVING TABLETS: A NOVEL DRUG DELIVERY SYSTEM. European Journal of Pharmaceutical and Medical Research. 2017,4(12), 161-172. ISSN 2394-3211.