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The insights on Oro-dispersible tablet

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ABSTRACT

Orodispersible tablets (ODTs) were the conventional product that disintegrates or dissolves into the buccal mucosa in less than 1mins in the absence of water and without chewing. They were first acquainted with the market during the 1980s, and end up one of the quickest developing subdivisions of the oral medication conveyance industry and their items are creating at an extraordinary rate. New orodispersible tablet innovations address numerous pharmaceutical and need of patients, extending from upgraded life-cycle the executives for reasonable medicating for pediatric, aged, and mental patients with trouble in swallowing. These supposedly affect about 35% of the all-inclusive community and related to various ailments like Parkinsonism, mental incapacity, motion sickness, obviousness, water inaccessibility, and so on. Other individuals possibly will face difficulties by utilizing control release solid oral product comprise the psychologically ill, partially developed patients, and rare patients those are unco-operative, on taking place diminished fluid consumption and are nauseated. To defeat such troubles, orodispersible tablets have been formulated. In this dosage form, the property of ODTs can be reached by the expansion of various additives such are super-the disintegrating agent is the main excipient. This has been motivated by both industry and academia to develop advanced orally dispersible products and advanced methodologies in the market. The ODTs are the most extensively implemented marketable products than others. The main purpose of this review paper is to provide the complete information of ODTs formulation.

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INTRODUCTION

During the last decade, the importance of the improvement of the orally disintegrating tablet has been massively extended as it has a significant influence on the comfortable of a patient. In spite of

increasing importance in the conventional release of drug delivery systems, the widely known medications they were administered to be absorbed, disintegrate, and discharge the medicament quickly in the GI Tract and still leftovers the dosage form of superior selection. DTs were core, or coated tablets are administered to disintegrate into the water giving a uniform distribution before administration. Therefore the appropriate selection of the disintegrating agent and its reliability of performance for improvement of such tablet formulations are critically important. The administrations of the medications to the older patients have turned into a major barrier in medication treatment, basically because of the difficulty in swallowing disability. ODT offers a benefit for people who have been facing trouble in administering. This has been accounted for dysphagia is communal amongst all groups of age and fur-

ther precise, patients with nausea, vomiting, motion sickness complications (Roy, 2016). Enhancing the better taste and flavor of ODTs will increase the appropriateness of bitter medications for numerous groups of the populace.

USFDA outlined **ODTs** as "A solid dosage form comprising of API that breakdown rapidly generally within 1 minute once located on the tongue." ODTs disintegration time usually varies from seconds to about a minute.

United States Pharmacopoeia (USP) approves the terminology of these dosage forms as ODTs. In recent times, EP has been made use of the word oro-dispersible tablet, which dissolves immediately and inside 3 minutes in the buccal cavity prior to swallowing. ODTs are also named as oro-dispersible, quick-disintegrating, mouth-dissolving, fast-dissolving, rapid melts, and porous tablets. Presently such tablets in market exit to treat numerous therapeutic disorders such are pre & post-operative pain, headache, nausea, vomiting, high blood pressure, etc. (Parfati *et al.*, 2018).

MATERIALS AND METHODS

Classification of ODTs

The ODT's are classified, as shown in Table 1.

Destination of oro-dispersible

Oro-Dispersible is recognized from control release sublingual tablets, buccal tablets, and lozenges, which want over a moment to break down in buccal mucosa. In the absence of water, a freeze-dried wafer is quickly disintegrated. To assure the stability for this dosage form physically, this needs single-dose packing. These wafers break down immediately and discharge drug in the buccal mucosa, which disperses in the salivation, and further, it is swallowed, and absorption of the drug takes place in GI-Tract.

An ODT once positioned in the buccal mucosa, which contains therapeutic excipients and breaks down quickly in the absence of water. The medication is discharged, breaks down in the salivation, then swallowed and absorbed in the GI-Tract. A rapidly break down tablet is a solid oral tablet that will swallow in the absence of water, which breakdown inside 60 sec when positioned in the buccal mucosa. The therapeutic excipients are dissolved and absorbed over the buccal membrane and GIT, which move across the systemic circulation. Little quantity of pre-gastric medicament absorption might evade the gastrointestinal system and metabolize by the enzymes and stomach acids (Kuchekar *et al.*, 2003).

Salient features of ODTs

1. Administration of dosage form to patients with difficulties in swallowing is simple.
2. Accurate in dose as compared to oral-liquids.
3. In the absence of water, the medication can be administered, helpful for people who are in the journey, and not have instant facilities of drinking water.
4. Certain medications were absorbed from the buccal cavity, pharynx, and esophagus by means of salivation move across the digestive system, and then the availability of drugs is expanded.
5. Absorption develops bioavailability by not experiencing the first-pass metabolism reduce the dose, and then enhanced scientific execution over the decreased undesirable effects.

Ideal-properties of oro-disintegrating tablets

The execution of ODTs relies upon the technology, which is utilized during their industrial process. The significant property of these tablets is the capacity to break down quickly and dissolve in salivation, thereby avoiding the requirement for water.

It should meet the below conditions

1. It should degenerates and break down within 60 seconds in the absence of water.
2. It must require enough ability to bear the conditions like the stiffness of the industrial process and post-manufacturing handling.
3. Must permit more doses filling.
4. Show low affectability to environmental conditions like temperature and humidity.
5. It is more precise dosing.
6. It should be convenient without friability worry.

Mouthfeel

It is a major property, and people must get medicine, which senses pleasant and sweetened.

Foaminess is added to help in the breakdown, and mouth-feel can be enhanced by reducing the "waterlessness" of a drug.

Friability

In request to enable ODTs to disintegrate in the buccal cavity, which are comprised of whichever

Table 1: ODTs Classification

	1st generation ODTs	2nd generation ODTs	3rd generation ODTs
Methodology	1. By freeze-drying process	1. wet granulation method 2. Drying the medication and excipients after compressing their wet mass	1. Dry granulation technique 2. Drying the mass containing the drug and saccharides were compressed
Advantages	Rapid disintegration of ODTs	Rapid disintegration of ODTs	1. Rapid disintegration of ODTs 2. Less friable than the first generation
Disadvantages	1. Handling was difficult because the tablets were very friable 2. Highly sensitive to moisture 3. No taste-masking compounds applied for bitter-tasting drugs 4. Low density and hardness	1. low hardness of tablets 2. High porosity Low density	1. High porosity 2. Low density 3. low hardness

extremely leaky or compacted to tablet by means of applying low compression force and cause the product friable are hard to deal with, frequently need specific peel-off blister packing. To defeat this kind of issue, a few organizations presented progressively strong types of fast dissolving tablets, for example, Wowtab and Dura Solve (Siddiqui *et al.*, 2010).

Advantages of orodispersible tablet

1. Quick drug therapy interference.
2. ODTs are considered to be the desired dosage form for Rapid drug delivery.
3. Medication is discharged rapidly from this dosage form and gets break up in the GIT tract without getting into the stomach; improved bioavailability can be accomplished.
4. ODTs are advantageous for administrating to a different category of patients from disabled, explorers, and busy people, who don't generally approach the water.
5. It creates great mouth feel property, which changes the impression of medication. This factor is valuable while formulating a dose for pediatric patients.
6. Enhanced patient compliance.
7. Delicate medicine for the acidic condition can be intended as ODTs.
8. No water required.

9. No chewing required.
10. Improved taste.
11. Improved stability.
12. Appropriate for conventional release studies.
13. Permits more doses filling.
14. Leave the least possible residue.
15. Cost-effective (Bandari *et al.*, 2008).

Disadvantages of Orodispersible tablets

1. These are highly hygroscopic, so care has to be taken while storage.
2. Dosage form, which is having very high doses, is challenging to formulate into Oro-dispersible.
3. Due to its porous structure, ODTs are highly fragile sometimes.
4. The safety and proper stabilization for a stable product that needs unit-drug packaging.
5. After taking ODTs special precautions must be taken, like eating and drinking may become restricted for some time (Abay, 2015).

Need for development of ODTs

The requirement for Noninvasive route persists is due to patients deprived acceptance and compliance with the current route of administration of drug regimes, the limited commercial scope for pharmaceuticals firms, and its product uses, in account to increase the cost of disease-organization.

Patient factors

1. Pediatrics and old aged people are having difficulties in administering or consumption of solid-orals.
2. Patients who are the concern of choking it is only because of unwilling to in the administration of the solid-oral formulation.
3. Terribly old-aged peoples might be not ready to administer a regular dosage of anti-depressant drugs.
4. Aged lady undertaking radioactivity treatment for a breast tumor is also too nauseating to administer H2-beta-blocker (Hirani *et al.*, 2009a).

Efficacy factor

Improved availability of the drug and quicker release of the drug are severe factors of those dosage-forms. Drug absorbed in the salivation of the buccal cavity, which affects the pre-gastric absorption from various dosage forms. In such cases, the drug was dissolved rapidly.

Oral mucosa, throat, and GI in all these areas absorption of various drugs. Some Pre-Gastric absorption evades 1st pass-metabolism and which might an excellent benefit in a medicinal product that endures an excellent interest in the metabolism of an internal organ (Pfister and Ghosh, 2005).

Manufacturing and marketing factors

Evolving innovates technologies for the drug delivery system and which help in growth for pharmaceuticals to persist, regardless of their growth size in the market. As the product loses its patent life, which is communal for pharmaceutical manufacturers to improve the medicinal product. A new dose permits an industrialist to improve commercial exclusiveness, distinctive product difference, business postponement, and prolong patent security while providing their patients with a new appropriate dosage form, which results in improved income.

Problems with current solid orals

1. Patients might experience the ill effects of tremors; in this manner, they may feel problems in taking fine particles and fluid medicine. In facing problems in swallowing, mental obstacles and adhering to throat might result in duodenal ulcer.
2. It will cause difficulty in the improvement of the muscular and sensory system for young adults

by facing problems in the incorporation of solid orals.

3. Fluid medicines are filled in multi-dose bottles: in this way, contented consistency in every dosage portion may not be kept up.

Challenges in formulating ODTs**Palatability**

Various medications stay unpleasant; solid-orals sometimes comprise the medicines in a palate taste screened form. The drug delivery system dissolves the drug in the patient's oral mucosa. Then their active therapeutic substance will come across to taste buds, and therefore, taste covering of the drug becomes a critical parameter for comfortable of the patient.

Mouthfeel

The ODTs after disintegration, particles formed must be very small, and it would not have adherence to any residue in the buccal cavity after oral administration with adding of flavoring and cooling agents like menthol will enhance mouth feel.

Mechanical strength

In request to enable ODTs to disintegrate in the buccal cavity, which are comprised of whichever extremely leaky or compacted to tablet by means of applying low compression force and makes the product friable are hard to deal with, frequently need specific peel-off blister packaging.

Hygroscopicity

So many oro-dispersible products were not able to maintain physical reliability under the standard conditions of temperature and humidity due to hygroscopic. Therefore, they need to protect the product from moisture, which involves the specialized product packaging.

Quantity of drug

The utilization of technologies for ODTs is restricted by means of the amount of drug incorporated in a single dose. Lyophilized drug products for which insoluble and soluble drugs dose should be below 400mg and 60mg. Therefore, the amount of drugs is very crucial for the development of oro-dispersible films or wafers.

Aqueous solubility

This parameter has more product development challenges, which are result in the formation of eutectic mixtures. In Further, they will cause the freezing point depression and leads to the development of glassy solid, which might breakdown during drying because of the loss of structure during the

sublimation process. By utilizing a matrix-forming substance, such collapses can be prevented (Hirani *et al.*, 2009b).

Excipients required for the formulations of oro-dispersible

The below excipients were required in the development of ODTs

Superdisintegrants

The pharmacists are required to develop and formulate fast disintegrating formulation by using various super disintegrating agents for the immediate release of the active ingredient. These agents are in effect at lower concentration and which have the higher dispersible capability and are more ineffective at Intra granularly.

It acts by the swelling mechanism, which leads to pressure release within the radial or outer direction. Further, it will cause a tablet to burst and result in an increase in the volume of granules to cause disintegration.

It is regularly used in tablet and capsule formulations to stimulate penetration of moisture and break down of matrix of formulation in fluids.

List of Super-disintegrants

1. Microcrystalline cellulose
2. Sodium starch glycolate
3. Crospovidone
4. Cross Carmellose Sodium
5. Pregelatinized starch
6. Calcium CMC
7. Modified corn starch

Mechanism of Super-disintegrants

The breakdown of the tablets into the small particles by various following mechanisms:

Capillary Action

Breakdown of the drug due to capillarity is the first stage. The tablet is placed into the suitable aqueous media than the media enters the tablet and which is substituted by air adsorbed on constituents. Further, this will deteriorates the inter-molecular bond and disperse the tablet into fine particles.

Swelling

In general, this mechanism was most widely accepted for the dispersion of tablets by swelling

with great porosity and which result in slow disintegration due to lack of sufficient swelling force. The particles of the tablet will swell and breaks up the matrix, swelling sets up, and localized stress spreads throughout the matrix.

Due to Heat of Wetting (Air Expansion)

Due to the heat discharging properties, disintegrants get wetted and local stress released because of air expansion, which results in the breakdown of the tablet into particles.

By Release of Gases

The chemist incorporates effervescent powder in a tablet blend prior to compression. Due to the wetting of the tablet, CO₂ is released within a tablet because of the reaction between HCO₃⁻ + CaCO₃ with citric acid. Therefore, the disintegration of the tablet takes place due to the release of pressure within the tablet.

Enzymatic Reaction

The enzymatic reaction occurs due to the enzymes available within the body act as disintegrants, and then these spoil the binding property of binder, which disintegrates.

Particle Repulsive Forces

In this mechanism, the non-swellable particle is used in the formulations which disintegrate tablet due to repulsive electric force within the particles and for this water is needed.

Due to Deformation

During compression of the tablet, the disintegrating agent particles become partial-misshapen particles that enter into the main structure after coming contact to aqueous media. These results in misshapen particle size increased and caused the breakdown of tablets (Gandhi *et al.*, 2011).

Bulking agents

These bulking agents act as filler, dilatant, and cost-effective, which is significant in the formulations of ODTs. It will develop the textural property, which improves the disintegration within the buccal cavity. The advised bulking materials for these ODTs would be more sweetening agents.

E.g. CaCO₃, MgCaCO₃, Mannitol, CaSO₄ etc.

Emulsifying Agents

This agent helps in fast disintegration and release of drug from the formulation by swallowing or in the absence of water or by devoid of chewing. It will be also helpful in improving the bioavailability and stabilize the unmixable blend.

Eg. PEG-Ester, Alkyl sulfates, Sucrose ester etc.

Sweetening agent

These agents act as filler or diluent or bulking agents, which show more water solubility, sugariness, and impart palate screening features.

Eg- NATURAL: Dextrose, Sucrose, Mannitol, Lactose.
ARTIFICIAL: Cyclamate, Aspartame, saccharin.

Flavoring agent

These agents will improve the taste, patient's comfort, and acceptance.

E.g.- Strawberry, Vanilla, Fruit essence, Peppermint oil, menthol etc.

Surface Active agents :

These agents will decrease the surface tension and improve the solubility.

E.g., SLS, Polyoxyethylene sorbitol fatty acid esters, etc.

Binders

These agents will provide cohesive strength to powdered materials, which leads to forming granules. Therefore, these agents help in maintaining the stability and integrity of the tablet.

E.g., HPMC, PVP, PVA.

Colorings Agents

These agents help in improving the organoleptic and appearance of the drug product. The examples of coloring agents are shown in Table 2.

Table 2: Examples of Coloring agent.

Fd & c approved color	Comman Name
Yellow 5	Tartrazine
Yellow 6	Sunset yellow
Red 3	Erythrosine
Red 40	Allura red
Blue 1	Brilliant blue
Blue 2	Indigotine
Green 3	Fast green

Lubricants

These agents are used to decrease the friction and prevent adhesion of tablet between the die walls. It also helps in the easy ejection of pills from the cavity and in the transport of drugs from the oral cavity to the GIT.

E.g., Talc, PEG 400, Paraffin, Mg-stearate, Zn-stearate, etc

Formulation methods of oro-dispersible

The common methodologies to manufacturing Oro-Dispersible are described as below

Spray drying

This method is widely used in pharma-industries and in biochemical procedures, which helps in the rapid ejection of the liquid and gives a porous or fine powder. The tablets were formulated by compression of dried spray powder, and disintegrating agents like sodium starch glycolate or Croscopovidone or Croscarmellose sodium were used to enhance the disintegration time and dissolution profile. Therefore, it shows the disintegration time of 20 seconds (Singh *et al.*, 2015).

Sublimation

In the conservative method, compression of volatile substance into tablets and these substances removed by sublimation process at the temperature range of 40⁰C- 60⁰C. Further, this results in a porous structure and gives 25 seconds of disintegration time (Ashish *et al.*, 2011).

Freeze drying

In this process, solvents were removed from the frozen product comprising structure developing substances at very low in temperature to remove adverse thermal reaction and which will cause a change in the stability of the drug. The products prepared by this technique were generally low in weight, which has high porousness, and that results in fast dissolution (Patel and Rajendra, 2012).

Molding

In this process, the blend mixed with solvent such are water and ethanol, and then this mixture was passed through a fine screen and molded into tablets under high pressure, which lead to improving the dissolution profile. Therefore, this method is also called has compression molding (Ramjiyani *et al.*, 2015).

Mass extrusion

In this method, the blended mixture was softened with a mix of solvent water-soluble PEG and methanol. This softened blend mixture was filled in the syringe and ejected to form a cylindrical product. This product is then made into small pieces by using a heated blade, which results in the formation of tablets (Neeraj *et al.*, 2014).

Direct compression

In this process, the powder blend is prepared by dry or wet granulation method, which is directly compressed into a tablet. These prepared tablets were more friable, disintegrate rapidly, and the cost is less compared to the conventional dosage form.

Melt granulation

In this technique, granules were formed in molten

form by adding waxy substances with M.P of 33⁰C to 36⁰C and HLB value of 9. These substances will improve the tablet resistance and which will help in the disintegration of tablets after melting in the oral cavity (Kuno *et al.*, 2005).

Phase transition process

In this process, tablets were formulated by compression of blend mixture comprising of sugar alcohols with high and low M.P and which will cause phase transition of sugar alcohols. Therefore, increased bonding between the particle and surface area of the tablet by lowering M.P of sugar alcohol.

Nanonization

In this technique size of the particle was decreased to Nanosize by wet-milling technology, and then these Nano drug particles were stabilized by surface adsorption. Further, these stabilized particles were incorporated into a metered-dose transdermal spray. Therefore, this methodology helpful in the fast dissolution of Nanoparticle for poorly water-soluble drugs and which leads to improvement in absorption, bioavailability, dose reduced, and cost-effective (Manyika *et al.*, 2016).

Effervescent Method

In this method, oro-dispersible were developed by reacting Na₂HCO₃ and citric acid with super disintegrating agents. Further, this mixture blend was heated at 80⁰C and compressed into the tablets.

RESULTS AND DISCUSSION

ODTS patented technologies

All methodology has various kind of mechanism, and these vary as follows below listed Strength of Finished product Mechanically

1. Stability of drug product and drug
2. Mouthfeel
3. palatability
4. The dissolution rate of the drug product in the buccal cavity.
5. The ability to swallow.

The listed below are Patented Technologies

Zydis Technology

Zydis system is an isolated freeze-dried pill wherein the drug is dissolved with the quick-dissolving material. When zydis formulations are situated into

the mouth, the freeze-dried constitution disintegrates instantaneous and does not require water for swallowing. To provide force during dealing with, polymers reminiscent of gelatin, dextran, or alginates are added. To obtain Crystallinity, good appearance, and hardness, saccharides are delivered. Water is used within the manufacturing approach to be a certain production of porous items to gain rapid disintegration. Exceptional gums are utilized to preclude sedimentation of dispersed drug particles in the industrial procedure. Glycine is delivered to restrict the shrinkage of zydis items during the freeze-drying process (Szuchaj and Nieuwenhuyzen, 2003).

Durasolv Technology

CIMA LABS patented this technology, and in this unit are comprised of drugs, lubricants, and bulking agents. Further, this unit is prepared by tablets compression machine and which had better rigidity. These prepared units are packed into blister packaging. This technology is good for those products which required less quantity of API (Gohel *et al.*, 2004).

Orasolv Technology

This technology is also developed and patented by CIMA LABS. This technology helps to mask the taste of drugs and which contains foam-forming disintegrating agents. Further, this powder blend compressed to form tablets at low compression forces for improving the disintegration time (Rish, 2004).

Wow tab Technology

This technology is developed without the use of water, so it is called Wow and which is patented by Yamanouchi pharmaceuticals. In this method, low and high stability saccharides were combined with API and which result in active, quickly dispersible tablets.

Flash Dose Technology

This technology comprises of the matrix, which is in self-binding shear form, and it is known as "floss," and these shear matrices were prepared by a process called flash heating.

Flash tab Technology

In this technology, API is made into the microcrystals. Then micro granules are formed due to various techniques such as micro-encapsulation, coacervation, etc. further; these granules were compressed to form tablets.

Oraquick Technology

This technology is also known as microsphere or micro mask technology, which is patented by KV

Pharmaceutical. This mainly enhances the taste and mouthfeel, and it doesn't use any kind of solvents for masking the taste. Then this results in the fast production of oro-quick tablets, which is suitable for heat-sensitive drugs.

Quick -Dis technology

In this technology, a quick-disintegration film was prepared in which the drug was loaded and placed on the surface of the tongue. This film was evaluated for disintegration time; the film with a thickness of 2 mm starts to break down when it comes in contact with water within 5 to 10 sec. Then, these dosage forms release its 50% of API below 30 sec and 95% within 60sec. This technology was developed and patented by Lavi pharma laboratories.

Nanocrystal technology

In this technology, the surface area of the particle was increased by reducing the size of particles, which will improve the dissolution. This can be achieved by utilizing the right Nanocrystal technology in which the particle size of Nano-crystal was less than 1000nm diameter. This size was achieved by blending the drug particles using the best-wet milling method (Kaushik *et al.*, 2004).

Melt Easetm technology

This is advanced technology in which tablets with the average size of 400 will disintegrate within 5 sec, and it was the best technology for improving the patient compliance and market by supplying the nutritional product at low cost for the elderly and children.

Dispersible tablet technology

In this technology, tablets were prepared by using a various super disintegrating agents such are sodium starch glycolate, Crospovidone, etc.; these agents will improve the dissolution profile and faster the disintegration of the drug particle by swelling and wetting mechanism of the drug product.

AdvaTab technology

In this technology, the lubricant is applied on the tablet surface by spraying during manufacturing, and it can be prepared by using less than 10-30 times hydrophobic lubricant and 30-40% harder than a conventional oral tablet. This type of tablet will not inhibit the entry of liquid when it contacts with salivation (Prabhu *et al.*, 2011).

Pharmaburst technology

In this technology self-coprocessed, excipients were used to develop the oro-dispersible tablets. The API used in this technology is up to 700 mg and pharmaburst concentration of 50-80%, which will

dissolve the drug product within 30-40 sec. Later during manufacture, dry blend of the drug is used and which are compressed into tablets (Bhupendra *et al.*, 2012).

Frosta technology

In this technology, plastic granules were prepared at the low force of compression and which will result in more porosity with the formation of hard tablets. These granules contain water penetration enhancers, plastic material, and binder. Later, plastic granules were formed, and these granules were compressed into a tablet (Kunchu *et al.*, 2013).

Lyon (Pharmalyoc)

In this technology, oil in water emulsion was poured directly into the blister cavities, and then the freeze-drying process takes place. During this process, added bulking agents to increase the thickness and avoid Non-homogeneity (Mehta *et al.*, 2010).

Evaluation of orodispersible tablets

Preformulation Studies

Angle of Repose

The powder blend was administration into the funnel, which flows freely on to the surface, and then height and radius of powder cone were measured and calculated for an angle of repose.

$$\tan \theta = \frac{h}{r}$$

Therefore $\theta = \tan^{-1} h/r$

Where: θ = angle of repose,

h = cone height

r = cone base Radius

The limits for the flow property of powder are shown in Table 3.

Table 3: Limits of Flow Properties powder

SL/No.	$\theta = \tan^{-1} h/r$	Flow type
1	<20	Outstanding
2	20-30	Good
3	30-40	Better
4	>40	Poor

Bulk Density

It is defined as the weight of the sample divided by the untapped volume and is conveyed as gm. / cm³.

$$BD = \frac{W}{Bv}$$

Where,

BD = Bulk Density

W = Sample weight

Bv = untapped or bulk volume

Tapped Density

It is the ratio of the weight of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for 100 times, and the tapped volume was noted. It is expressed in g/ml.

$$TD = \frac{W}{TV}$$

Where, W is the weight of powder

The TV is the tapped volume of the powder.

Void Volume

The volume of the space is called as the void volume "v."

$$V = BV - TV$$

Where, BV = Bulk volume (volume before tapping)

TV = True volume (volume after tapping)

Carr's index (or) % compressibility

It indicates the flow properties of the powder. It is expressed in %.

$$C.I = \frac{TD - BD}{TD} \times 100 \%$$

Where, TD is tapped density

BD is bulk density

The relationship between Carr's index and flowability is shown in Table 4.

Table 4: Relationship between Carr's index and Flowability

SL/NO	Carr's index	Flow Property
1	5 - 15	Outstanding
2	12 - 16	Good
3	18 - 21	Better
4	23 - 35	Poor
5	33 - 38	Very bad
6	> 40	Extremely bad

Hausner's ratio

A similarity index to show the flow properties of the powder can be explained.

$$HR = \frac{TD}{BD}$$

Where, TD is tapped density.

BD is bulk density.

Post-Compression studies

Tablet thickness

Thickness is recorded by using "Vernier Calipers," and which is estimated by taking ten tablets for measurement of thickness.

Weight variation

From the prepared batch, twenty tablets were taken randomly for weighing to check for variation of weight. The limits for weight variation as per IP are shown in Table 5

Friability

This test was done in the Electro lab Friabilator apparatus and where we take the weight of 10 whole tablets, note down the weight of tablets and perform the friability using Friabilator and report the weight of the tablet after 100 revolutions at 25 RPM (Narkhede et al., 2010).

$$\% \text{ Friability} = 1 - \left(\frac{\text{Final weight}}{\text{Initial weight}} \right) \times 100$$

Hardness (Crushing strength)

The hardness of the tablet is checked with hardness testers by keeping a tablet between the tester, and then a force is applied to break the tablet. The limit for the hardness of uncoated tablet was 3-5 kg/cm² (Daharwal et al., 2008).

Water absorption ratio

A tablet is placed on the paper, which is two times folded in a small Petri dish comprising water of 6 ml and which is checked for the time needed for complete wetting. Later, wetted tablets are reweighed and calculate the water absorption proportion by given below formula.

$$R = 100 \times \frac{W1 - W2}{W2}$$

Where,

W1: Tablet weight before absorption of water

W2: Tablet weight after absorption of water

Table 5: Weight Variation Specification as per IP

Average weight	% variation
≤ 80 mg	±10
≥ 80 mg to ≤ 250 mg	±7.5
≥ 250 mg	±5

Table 6: Brief details regarding Recent Research on ODTs

S.No	Drug (therapy category)	Method used	Excipients used	Result
1	Aceclofenac (Non-Steroidal Anti-Inflammatory Drug)	Direct compression	MMC, CCS, sodium starch glycolate,	Decreased Disintegration time, faster dissolution.
2	Nateglinide(anti hyperglycemic agent)	Direct compression	Pregelatinized starch, sodium starchglycolate, crospovidone.	Better patient compliance,
3	Celecoxib (NSAID)	Direct compression	Microcrystalline cellulose, crospovidone, ACDI sol	Increased Bioavailability
4	Rosu-vastatin (HMG-CoA reductase)	Dispersions of solid	Mannitol, sodium Starch glycolate, PEG-6000, Pregelatinized starch, Croscarmellose sodium.	Improve the rate of dissolution and solubility of the drug.
5	Cinnarizine (H1-antagonist receptor)	Sublimation	sodium saccharine , MMC, Croscarmellose sodium, sodium starch Glycolate, camphor.	Improve the bioavailability and Patient compliance and which will cause the rapid onset of action,
6	Promethazine chocolate(anti histamine)	Direct compression	Microcrystalline cellulose, camphor, crospovidone, mannitol, actress, β - cyclodextrin.	89% Drug release in 5 mins.
7	Domperidone (anti-emetic) and Omeprazole (a proton pump inhibitor)	Direct compression	Croscarmellose , Ac-Di-Sol, Kollidon CL, Sodium starch glycolate	Poor aqueous solubility
8	Metformin hydrochloride(oral antidiabetic biguinide agent,)	Direct compression	MCC, Mannitol, Croscarmellose Sodium, crospovidone, sodium starch glycolate	Within 30mins, 98.7% drug was released.
9	Carbamazepine (tricyclic antidepressants)	Solid dispersions	SLS, PEG-6000, PVP, MCC, Croscarmellose Sodium , Aspartame	Improved bioavailability, better patient compliance.
10	Lisinopril (ACE inhibitors)	Direct compression	Croscarmellose Sodium, Crospovidone, Sodium starch glycolate, Mannitol	Within 30 mins, the Drug was released is 99.99% and which will be enhanced dispersible time
11	Oxcarbazepine (NSAID)	Wet granulation	Avicel pH 102, Aerosil	Enhanced dissolution
12	Valsartan (antihypertensive)	Direct compression	AC-DI-SOL, Sodium saccharine, Crospovidone, Sodium starch glycolate, MCC	Greater bio availability,

Uniformity of dispersion

Place two tablets in 100ml of water and stir gently until completely dispersed. A smooth dispersion is obtained, which passes through a sieve with a nominal mesh aperture (sieve no. 22).

Disintegration time

This test was carryout by placing six tablets into the basket each one and maintain at 37⁰C.

According to the E.P, the quick disintegrating or Orodispersible tablets ought to disintegrate within 3 minutes while not leaving any residue on the screen. However, The basket is thus positioned within the liquid that it contains only 6 ml of the liquid. The assembly is supported with a heater to take care of temperature at 37°C and a magnetic stirrer. DT is noted at 25 pm. One of the modest approaches is to take 6ml of simulated saliva in a measuring cylinder and insert the tablet in it. The liquid is neither shaken nor stirred, and DT is noted (Morita *et al.*, 2002).

In vivo disintegration time

A panel of healthy human volunteers is used to perform this test. The time taken by volunteers to disintegrate by retaining the tablet in the mouth is noted.

Taste/ Mouth sensation

The product received by the patients should feel pleasant. This test is carried out by taking one tablet from each batch for the taste by retaining the tablet on the tongue.

To analyze the mouth sensation, panels of 5 healthy human volunteers are utilized.

Sample equivalent to 40 mg is placed in the mouth for 10 seconds, and the taste is recorded instantly for 10 secs, 1, 2, 4, and 6 minutes.

Volunteer's opinion scores are given i.e. 0 = good, 1 = tasteless, 2 = slightly bitter, 3 = bitter, 4 = awful.

Dissolution test

The dissolution test for oro-disintegrating tablets is the same as that of standard tablets. The USP 2 (paddle) at a 50 RPM paddle speed is used to perform this test.

The USP 1 (basket) apparatus is less often used due to the specific physical properties of tablets. (Yaheya and Ismail, 2009).

Clinical studies

To do clinical studies for oro-dispersible tablets. *In vivo* studies are done to study the behavior of drugs within the oral, esophageal tract, their pharmacokinetics, adequacy, and efficiency. By using

gamma-scintigraphy were investigating the residence time within the mouth and stomach through the esophageal tract. The transit time of esophageal and stomach evacuating was compared with the standard tablets and capsules. The fast disintegration tablets were examined and shown improves in the pharmacokinetics properties with standard solid orals (Bruna *et al.*, 1998; Daharwal *et al.*, 2008).

Counseling points for ODTs

The registered pharmacist is advancing in the various technologies and guiding their patients on how to administer the drug dose for their first time. Most of the patients were not known of how to take the orodispersible tablet and which dissolves within the oral cavity make the patient in shock and shows the rapid onset of action. Patents clear their doubts with the pharmacist to avoid misunderstanding or confusion. These formulations were rapid dissolves in the absence of water and used the saliva for a breakdown of the drug. If the volume of saliva is low, then it will slow down the disintegration and decreases the bioavailability of the drug product.

This dosage form can be easily utilized by children who don't have teeth and patients who are feeling difficulties in chewing. Pharmacists should clearly state the difference between effervescent tablets and dispersible tablets (Hirani *et al.*, 2009a).

Recent research on ODTs

Various studies have been reported the formulation and evaluation of ODTs of various drugs for different purposes are shown in Table 6

CONCLUSIONS

The overview of ODT formulation has resolved a number of the issues encountered in the administration of medication to the pediatric and aged patient, which constitutes a large proportion of the world's population. Nowadays, ODTs are available in the market and have OTC products to treat flu symptoms, cold and allergies. These ODTs were formulated as full porous in the structure of the tablet for the rapid dissolution of the tablet matrix with a pleasant taste and with appropriate mechanical strength. Therefore for the rapid disintegration of tablets, super disintegrating agents were used in different concentrations depending on the drugs. The research work is still going on, and more number of manufacturers are formulating fast-dissolving tablets. More number of ODTs products was marketed and which are expressed by utilizing advanced innovative technologies. Therefore, ODTs was formulating for more number of drugs and for various treatments of disease in the future.

Table 7: Brief details regarding Recent Research on ODTs (Continued From Table 6)

S. No	Drug (therapy category)	Method used	Excipients used	Result
13	Etoricoxib (NSAID)	Direct compression	Urea, Croscarmellose, Avicel	rapid dissolution, enhance patient compliance, quick DT
14	Granisetron HCL	Direct compression	Croscarmellose, Crospovidone	Enhanced Dissolution rate
15	Ramipril (Antihypertensive)	Wet granulation	Sodium bicarbonate, Polyvinyl pyrrolidone, Citric acid, Mannitol	Rapid disintegration and dissolution
16	Rizatriptan benzoate (Serotonin 5-HT receptor agonist)	Mass extrusion	Crospovidone, Eudragit EPO, Croscarmellose sodium, Sodium starch glycolate, Pearlitol SD200	Complete taste masking, rapid disintegration and dissolution
17	Ebastine (2 nd generation non-sedating H1 - receptor antagonist)	Sublimation	PVP, Camphor, Mannitol, Sodium saccharine, Ammonium bicarbonate, Microcrystalline	Improved dissolution, faster disintegration (<1 min)
18	Clonazepam (Antiepileptic)	Direct compression	Crospovidone, Croscarmellose, Directly Compressible Mannitol, Microcrystalline cellulose	Enhanced patient compliance
19	Isoxsuprine hydrochloride (Vasodilator)	Direct compression	Microcrystalline cellulose, Crospovidone, β -cyclodextrin, Ac-di-sol, Sodium starch glycolate, Mannitol	High release rate
20	Levocetirizine hydrochloride (Non-sedative anti-histaminic)	Direct compression	Croscarmellose, Primojel, Crospovidone, MCC	Improved bio availability, rapid onset of action
21	Meclizine hydrochloride (Antiemetic)	Direct compression	Crospovidone XL 10, Avicel pH 102, Pearlitol SD 200	Rapid disintegrate-on, quick onset of action
22	Montelukast Sodium (Antineoplastic)	Direct compression	Crospovidone, Sodium starch glycolate, Mannitol, Microcrystalline cellulose	Enhanced
23	Salbutamol Sulphate (β 2 receptor agonist)	Direct compression	Microcrystalline Mannitol-D, cellulose, Propyl cellulose, Primogel, L-hydroxy	Rapid dissolution and Rapid onset of action
24	Telmisartan (Antihypertensive)	Direct compression	Skimmed milk powder, Poloxamer-188, Crospovidone	Better solubility, Rapid disintegration and high dissolution rate

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