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A Review on Formulation and Evaluation of Orodispersible Tablets

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Abstract
Oral route is presently the gold standard in the pharmaceutical industry where it is regarded as the safest, most economical and most convenient method of drug delivery resulting in highest patient compliance. Oral delivery of active ingredients includes a number of technologies, many of which may be classified as Orodispersible tablets (ODTs). Orodispersible dosage forms have lured the market for a certain section of the patient population which includes dysphagia, bed ridden, psychic, and geriatric patients. Moreover, Orodispersible tablets shows increased bioavailability as compared to conventional dosage forms. Advancements in the technology arena for manufacturing these systems includes the use of freeze drying, cotton candy, melt extrusion, sublimation, direct compression besides the classical wet granulation processes. This has encouraged both academia and industry to generate new orally disintegrating formulations and technological approaches in this field. This article attempts at discussing the ideal characteristics, advantages and disadvantages, formulation aspects, formulation technologies and future potential of ODTs.

Keywords
Dysphagia, Psychic, Geriatric Formulation technologies, Orodispersible tablets, pharmaceutical industry.

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INTRODUCTION:
Orodispersible tablet system can be defined as a tablet that disintegrates and dissolves rapidly in saliva within few seconds without need of drinking water or chewing [2]. Orally disintegrating tablets have better patient acceptance and compliance and may offer improved biopharmaceutical properties, efficacy and increased bioavailability compared with conventional oral dosage forms [1] They obviate the problem associated with conventional dosage forms, it has benefits like desired hardness, dosage uniformity, extremely easy administration and since no water is required for swallowing these tablets are suitable for geriatric, pediatric and travelling patients. These tablets display a fast and spontaneous deaggregation in the mouth, soon after it comes in contact with saliva, dissolving the active ingredient and allowing absorption through all possible membrane it comes in contact during deglutition [3].

Today, ODTs are more widely available as OTC products for the management of many conditions such as allergies, cold, and flu symptoms. [4] The presence of a highly porous surface in the tablet matrix is the key factor for rapid disintegration of ODT. [5]

To improve the porosity, volatile substances such as subliming agents can be used in tableting process [6],[7], [8] which sublimated from the formed tablet. Also freeze-drying technique is used to form a highly porous ODT. [9], [10]. In recent past, several new advanced technologies have been introduced for the

formulation of orodispersible tablets with very interesting features like extremely low disintegration time, exceptional taste masking ability, pleasant mouth feel and sugar free tablets for diabetic patients.[11], [12]

Advantages of Orodispersible Tablets [13[, [14]:

1. Rapid disintegration of tablet results in quick dissolution and rapid absorption which provide rapid onset of action
2. Allows high drug loading
3. Alternative to liquid dosage form
4. Formulation is cleared from the esophagus especially in the supine position without lodging or sticking to it when swallowed, thus offering improved safety
5. Cost effective
6. No risk of choking
7. New business opportunities; line extension, exclusively of product promotion and patent life extension.
8. Administration to the patients who cannot swallow, such as the elderly, stroke victims, bedridden patients, patients affected by renal failure and patients who refuse to swallow such as pediatric, geriatric and psychiatric patients.
9. Convenient for administration and patient compliant for disabled, bedridden patients and for travelers and busy people who do not always have access to water.
10. Good mouth feel property helps to change the perception of medication as bitter pill particularly in pediatric patients.

Disadvantages Of Orodispersible Tablets: [14],[15],[16]

1. Hygroscopic in nature.
2. Low amount of drug can be incorporated in each dose.
3. Sometime it possesses mouth feeling.
4. Highly fragile sometimes.
5. ODT requires special packaging for proper stabilization and safety of stable product.
6. Eating and drinking may become restricted.

Ideal characteristics of Orodispersible Tablets: [17],[18]

1. Not require water to swallow and should dissolve or disintegrate in the mouth within a few seconds.
2. High drug loading
3. Be compatible with taste masking and other excipients
4. Have a pleasing mouth feel
5. Leave minimal or no residue in the mouth after oral administration
6. Exhibit low sensitivity towards environmental conditions such as humidity and temperature
7. Be adaptable and amenable to existing processing and packaging machinery.

Suitability of drugs for Orodispersible tablets: [19]

For developing ODT of a specific drug several factors should be kept forth while selecting drug, excipients and formulation method. These are as follows: Dugs to be used for sustained action are not suitable candidate for FDT. Drugs having very disagreeable taste are not suitable like clopidogrel. Patients suffering from Sjogren's syndrome and those with less saliva secretion and not suitable for ODT dosage form. Drugs of very short half-life and requiring frequent dosing are not appropriate candidate. Patients on anticholinergic therapy are not suitable for ODT. Drugs showing altered pharmacokinetic behavior if formulated in such dosage form with respect to their conventional dosage form are not suitable, like selegiline, apomorphine and buspirone. Drugs producing considerable amounts of toxic metabolites on first pass metabolism and in GIT and having substantial absorption in oral and pre-gastric areas are good candidates. Drugs permeable to upper GIT and oral mucosal epithelial cell lining are considered good candidates for ODT.

CHALLENGES IN FORMULATION OF ODTs: [5]

1. Disintegration time and Mechanical Strength

ODTs are formulated to obtain disintegration time usually less than a minute and actual disintegration time that patient can experience ranges from 5 to 30 s. The standard procedure of performing disintegration test for these dosage forms has several limitations and they do not suffice the measurement of very short disintegration times. The disintegration test for ODT should mimic disintegration in mouth with in salivary contents. While doing so, maintaining a good mechanical strength is a prime challenge. Many ODTs are fragile and there are chances that such fragile tablet will break during packing, transport or handling by the patients. Tablets based on technologies like Zydis need special type of packaging. It is very natural that increasing the mechanical strength will delay the disintegration time. So, a good compromise between these two parameters is always essential. [5], [14]

2. Taste-Masking

Taste masking of drug may be achieved with preventing the exposure of drug to the tongue through processing or adding competing taste-masking agents. Exposure of solubilized drug to the oral cavity can be prevented by encapsulation in polymer systems or complexation. The approaches are as follows: [20]

1. Layering the drug onto inert beads using a binder followed by coating with a taste-masking polymer. [20]

2. Granulating the drug and coating with a taste masking polymer. [21], [22]
3. Spray drying the drug dispersed or dissolved in a polymeric solution to get taste-masked particles. [23]
4. Complexation by the use of inclusion in cyclodextrins. [24], [25]
5. Psychological modulation of bitterness. [20]
6. Coacervation to form microencapsulated drug within a polymer. [26]
7. Formation of pellets by extrusion spheronization [21]

3. Sensitivity to environmental conditions: [5], [14]

ODTs generally should exhibit low sensitivity to environment conditions such as humidity and temperature as most of the materials used in ODTs are meant to dissolve in minimum quantity of water.

4. Mouth Feel: [5],[14]

ODTs should not disintegrate into larger particles in the oral cavity. The particles generated after disintegration of then ODTs should be as small as possible. ODTs should leave minimal or no residue in mouth after oral administration. Moreover, addition of flavours and cooling agents like menthol improve the mouth feel.

5. Cost: [5],[14]

The technology used for ODTs should be acceptable in terms of cost of the final product. Methods like Zydis and Orasolv that require special technologies and specific packaging increase the cost to a remarkable extent.

TECHNIQUES USED IN PREPARARTION OF ODTs:

1. Freeze Drying/ Lyophilization: [14],[19],[27],[28]

It is a pharmaceutical process that allows the drying of heat sensitive drugs and biological under low temperature by the application of vacuum to remove water by sublimation. Drugs are dissolved or dispersed in aqueous solution of a carrier, transferred to preformed blister packs and subjected to nitrogen flush to freeze out, then placed in refrigerator to complete the process. Characteristics of lyophilization techniques are, they possess high porosity and specific surface area, and gets dissolve rapidly in mouth presenting high drug bioavailability. Formation of porous product in freeze-drying process is exploited in formulating MDTs. Lyophilization is a process, which includes the removal of solvent from a frozen suspension or solution of drug with structure-forming additives. Freeze-drying of drug along with additives imparts glossy amorphous structure resulting in highly porous and lightweight product. The resulting tablet has Rapid disintegration and dissolution when placed on the tongue and the freeze-dried unit dissolves instantly to release the drug.

Advantages: More rapid dissolution than other available solid products.

Disadvantages: Major drawback of this system is high cost, time consuming procedure and fragility, making conventional packing inappropriate for packing this dosage form and stability issues under stress condition. Ahmed I.S. et al [28] prepared ODTs by freeze-drying an aqueous dispersion of Nimesulide containing a matrix former, a sugar alcohol, and a collapse protectant. Development of a lyophilized orally disintegrating tablet (ODT) enhanced the in vitro dissolution and in vivo absorption of Nimesulide, a drug with poor solubility and poor bioavailability.

2. Spray Drying: [29]

This technique is based on a particulate support matrix, which is prepared by spray drying an aqueous Composition containing support matrix and other components to form a highly porous and fine powder. This then mixed with active ingredients and compressed into tablets. Super disintegrants (such as Ac-Di- Sol, Kollidon CL, sodium starch glycolate), diluent (mannitol) along with sweetening agent (aspartame) were used in the formulation of tablets. The tablets were evaluated for hardness, friability, water absorption ratio, disintegration time (DT) and in vitro drug release. Using the same excipients, the tablets were prepared by direct compression and were evaluated in the similar way. Maximum drug release and minimum DT were observed with Kollidon CL excipient base as compared to tablets prepared by direct compression, showing the superiority of the spray dried excipient base technique over direct compression technique.

Advantages:

Advantages of the spray-drying method is this method gives rapid dissolution (within 20 seconds) when dosage form gets in contact with the aqueous medium. [29]

3. Molding [31]**:**

Tablets formed by molding process are highly porous in structure, resulting in high rate of disintegration and dissolution. This process includes moistening, dissolving, or dispersing the drugs with a solvent then molding the moist mixture into tablets by applying lower pressure in compression molding, but always lower than the conventional tablet compression. The powder mixture may be sieved prior to the preparation in order to increase the dissolution. Molded tablets have low mechanical strength, which results in erosion and breakage during handling.

Advantages [32]:
Because the dispersion matrix is, in general, made from water-soluble sugars, moulded tablets disintegrate more rapidly and offer improved taste. These properties are enhanced when tablets with porous structures are produced or when components that are physically modified by the moulding process are used.

Disadvantages [32]:
Moulded tablets typically do not possess great mechanical strength. Erosion and breakage of the moulded tablets often occurs during tablet handling and when blister pockets are opened.

4. Sublimation [33]:
Sublimation has been used to produce ODTs with high porosity. A porous matrix is formed by compressing the volatile ingredients along with other excipients into tablets, which are finally subjected to a process of sublimation. Inert solid ingredients with high volatility (e.g., ammonium bicarbonate, ammonium carbonate, benzoic acid, camphor, hexamethylenetetramine, naphthalene, phthalic anhydride, urea and urethane) have been used for this purpose. Solvents such as cyclohexane and benzene were also suggested for generating the porosity in the matrix.

Advantages [34]:
Kumar R et al developed mouth dissolving tablets of fenofibrate by using sublimation technique using menthol, camphor, ammonium bicarbonate and thymol as sublimating agent. Sublimation technique using vacuum oven was be an effective alternative approach to use of more expensive adjuvant and sophisticated instruments in the formulation of mouth dissolving tablets. The wetting time or simulated saliva penetration was observed to be very fast. The total drug from the optimized batch was found to be released within the first ten minutes of dissolution study. These tablets rapidly dissolved (within 10-20 sec) in saliva. The prepared tablet gives benefit in terms of patient compliance, low dosing, rapid onset of action, increased bio-availability, low side effect and good stability which make these tablets popular as a dosage form for the treatment of hyperlipidemia.

5. Mass Extrusion [35]:
In this technique, a blend of active drug and other ingredients is softened using solvent mixture of water- soluble polyethylene glycol, using methanol and then the softened mass is extruded through the extruder or syringe to get a cylinder of product, which is finally cut into even segments with the help of heated blades to get tablets. The dried cylinder can be used to coat the granules of bitter tasting drugs and thereby masking their bitter taste.

Advantages [36]:
Mask bitter taste by coating the granules. Mansing G. Patil et al prepared orally disintegrating tablets of Tramadol hydrochloride for achievement of quick onset of action of the drug. An attempt was to prepare bitterless orally disintegrating tablet using Eudragit E 100 as a taste masking agent. Mass extrusion was the technique used for preparing taste masked granules and tablet was prepared using superdisintegrants like crospovidone, croscarmellose sodium and sodium starch glycolate. The extrusion technique represents a novel application of polymer processing technology to prepare pharmaceutical dosage forms. The process involves embedding a drug in a polymeric carrier while shaping the composite material to form a pharmaceutical product. The drug release from orally disintegrating tablets increased with increasing concentration of superdisintegrants and was found to be highest with formulations containing Crospovidone.

6. Direct Compression [37]:
Direct compression represents the simplest and most cost-effective tablet manufacturing technique. This technique can now be applied to preparation of ODT because of the availability of improved excipients especially super disintegrants and sugar-based excipients.

a) Super Disintegrants [37]:
In many orally disintegrating tablet technologies based on direct compression, the addition of superdisintegrants principally affects the rate of disintegration and hence the dissolution. The presence of other formulation ingredients such as water-soluble excipients and effervescent agents further hastens the process of disintegration.

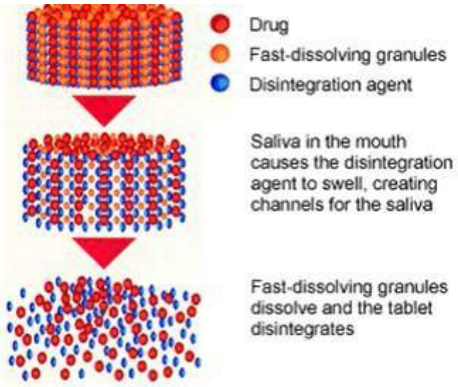

Fig 1: Basic mechanism of Super disintegrants.

MECHANISMS OF SUPERDISINTEGRANTS [37]:

There are four major mechanisms for tablet disintegration as follows:

1) Swelling:

Although not all effective disintegrants swell in contact with water, swelling is believed to be a mechanism in which certain disintegrating agents (such as starch) impart the disintegrating effect. By swelling in contact with water, the adhesiveness of other ingredients in a tablet is overcome causing the tablet to fall apart.

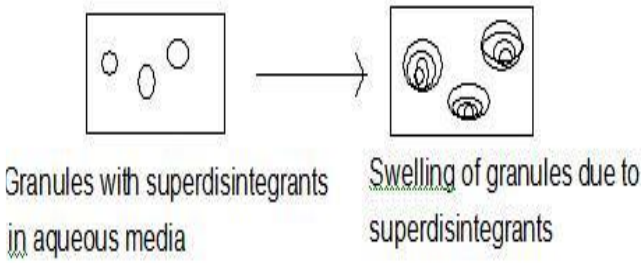

Fig. 2 Mechanism of superdisintegrants by swelling

2) Porosity and capillary action (wicking):

Tablet in the aq. Media leads to penetration of the medium into tablet and thus replacement of air adsorbed resulting in weakening of intermolecular bond and breaking of tablet into fine particles.

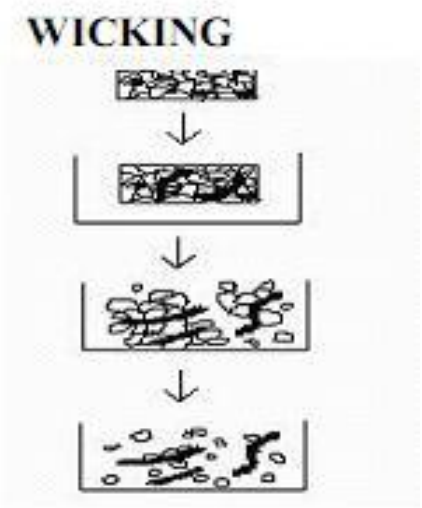

Fig. 3 Mechanism of superdisintegrants by Porosity and capillary action (wicking).

3) Due to particle-particle repulsive forces: The electric repulsive forces b/w particles responsible for disintegration. It is secondary to wicking.

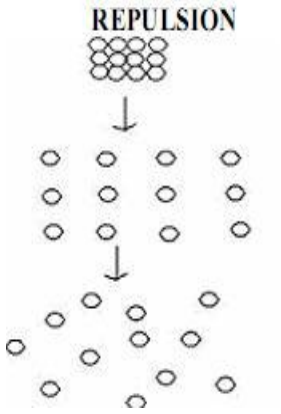

Fig. 4 Mechanism of superdisintegrants due to particle repulsive forces

4) Due to deformation: During tab. compression, disintegrated particles get deformed and in contact with aq. media returns to normal structure (inc. in size). Eg: starch.

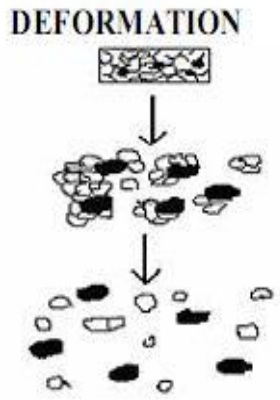

Fig. 5 Mechanism of superdisintegrant due to deformation

b) Sugar Based Excipients [37]:

This is another approach to manufacture ODT by direct compression. The use of sugar-based excipients especially bulking agents like dextrose, fructose, isomalt, lactilol, maltilol, maltose, mannitol, sorbitol, starch hydrolysate, polydextrose and xylitol, which display high aqueous solubility and sweetness, and hence impart taste masking property and a pleasing mouthfeel. Mizumito et al have classified sugar-based excipients into two types on the basis of molding and dissolution rate. Type 1 saccharides (lactose and mannitol) exhibit low mouldability but high dissolution rate. Type 2 saccharides (maltose and maltilol) exhibit high mouldability and low dissolution rate.

Table 1: List of common superdisintegrants [38]:

Superdisintegrants	Example of	Mechanism of action	Special comment
Crosscarmellose® **Ac-Di-Sol®**	Crosslinked cellulose	-Swells 4-8 folds in < 10 seconds. -Swelling and wicking both.	-Swells in two dimensions -Direct compression or granulation
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.
Alginic acid NF Satialgine®	Cross linked alginic acid	-Rapid swelling in aqueous medium or wicking action	-Promote disintegration in both dry or wet granulation.
Soy polysaccharides Emcosoy®	Natural super disintegrant	————————	-Does not contain any starch or sugar. Used in nutritional products.
Calcium Silicate		-Wicking action	-Highly porous -Light weight -Optimum concentration is between 20-40 %

Advantages [14]:
It is cost effective due to low manufacturing cost, conventional equipment and limited number of processing steps.
Disadvantages [14]:
Differences in particle size and bulk density b/w the drug and diluents may lead to stratification within the granulation. Large dose may present problem if it is not easily compressible by itself.
7. Phase transition process [39]:
Kuno et al. [40] investigated this process by compressing powder containing two sugars alcohols. One with high and another with low melting point, and they are heated at a temperature between their melting point and then compressed finally in order to get the tablets. Example of sugar alcohols are erythriol (m.p. 122°C), xylitol (m.p. 93-95°C), trehalose (97°C), and mannitol (166°C). After heating, tablet hardness was increased due to an increase in interparticle bonds or the bonding surface area in tablets induced by phase transition of lower melting point sugar alcohol.
8. Cotton Candy Process [40]:
Cotton candy process involves the formation of matrix of polysaccharides by simultaneous action of flash melting and spinning. This candy floss matrix is then milled and blended with active ingredients and excipients after recrystallization and subsequently compressed to mouth dissolving tablets. It can accommodate high doses of drug and offers improved mechanical strength.
Advantages: We can accommodate large doses of drugs by using this technique. Tablets prepared by this method show the improved bioavailability.
Disadvantages: Thermolabile drugs cannot be formulated by using this technology because of high process temperature.
9. Nanonization [40]:
In this method by using wet milling technique the size of the drug milled into nano size. This milled nano sized drug particles are stabilized against agglomeration by surface absorption on selected stabilizers and this is formulated into mouth dissolving tablets. This method is mostly employed for water soluble drugs for increasing the solubility of the drug which leads to increased bioavailability of the drug.
Advantages:
Cost effective manufacturing process.
Conventional packaging due to exceptional durability and wide range of doses
Patented Technologies:
Zydis Technology [42]
Zydis is a one-of-a-kind freeze-dried tablet that has the pharmaceutical physically trapped or dissolved inside a matrix of quickly dissolving carrier material. When patients put zydis pills in their mouths, the freeze-dried structure rapidly disintegrates, and they do not need water to consume them. The zydis matrix comprises a mix of components that collaborate to achieve various objectives. Polymers such as gelatin, dextran, or alginates add strength and resilience during handling. These combine to produce a glossy amorphous structure that adds stability. Zydis pharmaceuticals are wrapped in blister packs to preserve the formula from environmental dampness.
OraSolv and DuraSolv Technology [43]:
OraSolv technology (Cima Labs) produces tablets by low compression pressure. It uses an effervescent disintegration pair that releases gas upon contact with water. The widely used effervescent disintegration pairs usually include an acid source and a carbonate source. The acid sources include citric acid, tartaric acid, malic acid, fumaric acid, adipic acid, and succinic acids. The carbonate sources include sodium bicarbonate, sodium carbonate, potassium bicarbonate and potassium carbonate. The carbon dioxide evolved from the reaction may provide some “fizzing” sensation, which is a positive organoleptic sensation. The amount of effervescent agent is in general about 20–25% of the total weight

of the tablet. Because of the soft and fragile nature of OraSolv tablets, a special packaging system, known as PakSolv, was developed to protect the tablets from breaking during transport and storage. PakSolv is a "dome-shaped "blister package that prevents the vertical movement of the tablet within the depressions, because the diameter of the lower portion of the dome is too narrow to accommodate the tablet. PakSolv also offers light, moisture, and child resistance. As a second-generation technology, the DuraSolvR technology was developed by Ciba to provide stronger tablets for packaging in blisters or bottles.

The key ingredients in this formulation are non-direct compression filler and lubricant. The particle size of the non-direct compression filler is preferably between about 20 and 65 µm, while for direct compressible fillers at least 85% of the particles are over 100 µm in size. These non-direct compression fillers, such as dextrose, mannitol, sorbitol, lactose, and sucrose, have the advantage of quick dissolution and avoid some of the gritty or sandy texture usually present in direct compressible versions of the sugar. The amount of nondirect compression filler is usually about 60–95% of the total tablet weight. The tablets have low friability, which is about 2% or less when tested according to the USP, and the hardness of the tablets is at least about 15–20 N. The disintegration time is less than 60 seconds. It is interesting to note that in comparison with the conventional tablet formulations, higher amounts of hydrophobic lubricants, such as magnesium stearate, can be added to the formulation with non-direct compression fillers as the main component. About 1–2.5% of lubricant can be added to the formulation, compared with 0.2–1% of lubricant in conventional tablets. The lubricant blending times can also be increased to 10–25 minutes or longer. Relatively modest compressive force is needed to compress the formulation. This method can produce tablets by the direct compression method and use conventional tableting methodologies and conventional package equipment. Thus, the production cost is significantly decreased.

Flashtab Technology [44]:

Flash tab technology is patented by Prographarm labs in which the preparation of rapidly disintegrating tablets contains active ingredients in the form of microcrystals. By using conventional techniques like simple pan coating methods, coacervation, microencapsulation and extrusion spheronization drug microgranules are prepared. Here disintegration time is less than one minute and good mechanical strength.

Flashdose Technology [44]:

By using "Nurofen meltlet" technology ODT tablet is prepared which is the first product launched by Bioavail Corporation. This technology uses unique mechanism of spinning that gives a floss like crystalline structure which resembles cotton candy process. Tablets are manufactured by using shear form matrix which contains fibrous polysaccharides that are compressed to form fine sugar fibres which disintegrates rapidly when comes in contact with saliva. The tablets produced by this method are soft, friable, moisture sensitive and have high surface area for dissolution, so disintegrates within few seconds.

Wowtab Technology:

This technology is patented by Yamanochi Pharmaceutical company, in this technology WOW means "Without water". In this tablet formulation two different types of saccharides are combined, such as saccharides with high moldability of hardness more than 2 kg and with low moldability with hardness 0-2kg [14]. Saccharides with high moldability (maltose, mannitol, sorbitol and oligosaccharides) is combined with low moldability (lactose, glucose, mannitol, xylitol) and compressed into tablets [45]. With the help of these combination of saccharides fast dissolution rate and adequate hardness can be achieved. In WOW tab formulation, because of its significant hardness it is more stable to environment. In this technology a good taste masking agent is used to produce good mouth feel by use of patented smooth melt action [46], [47].

Quickdis Technology:

In this technology formulation is kept on tongue to release the drug for local and systemic absorption. If the film with 2mm thickness breaks within 5-10seconds when brought into contact with water it is the typical disintegration time. If the 2mm thickness film breaks or dissolves around 30seconds when brought into contact with aqueous media then it is typical dissolving time and the typical release profile of active ingredient within 30 seconds is 50% and within 1 minute is 95. [32],[46]

Oraquick Technology:

Patented taste masking technology is used in oraquick technology which do not utilize any solvents for taste masking that leads to more efficient production. This technology is suitable for heat sensitive drug because this technology is processed using low heat. KV Pharmaceuticals claims "Micromask Technology" which is superior mouth feel technology than other taste masking methods [48].

Ziplets/advatab [32]:

This technology is patented by Pessano con Bornago, Italy. It utilizes water-insoluble ingredient combined

with one or more effective disintegrants to produce ODT with improved mechanical strength and optimal disintegration time at low compression force. This technology handles high drug loading and coated drug particles and does not require special packaging, so they can be packed in push through blisters or bottles.

Evaluation of Orodispersible Tablets:

Weight Variation [3], [49]:

With a tablet designed to contain a specific amount of drug in a specific amount of tablet formula, the weight of the tablet being made is routinely measured to help ensure that a tablet contains the proper amount of drug. In practice, composite samples of tablets (usually 10) are taken and weighed throughout the compression process. The composite weight divided by 10, however, provides an average weight but contains the usual problems of averaged values. Within the composite sample that has an acceptable average weight, there could be tablets excessively overweight or underweight. To help alleviate this problem the United States Pharmacopoeia (USP)/National Formulary (NF) provides limits for the permissible variations in the weights of individual tablets expressed as a percentage of the average weight of the sample. The USP weight variation test is run by weighing 20 tablets individually, calculating the average weight, and comparing the individual tablet weights to the average. The tablets meet the USP test if no more than 2 tablets are outside the percentage limit and if no tablet differs by more than 2 times the percentage limit. The weight variation tolerances for uncoated tablets differ depending on average tablet weight

Table 2: Weight Variation Specification as per IP

Average weight of tablet	% Deviation
80 mg or less	± 10
More than 80 mg but less than 250 mg	± 7.5
250 mg or more	± 5

Friability [50]:

Friability of the tablet determined using Roche friabilator or Electro lab friabilator. This device subjects the tablet to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping a tablet at I height of 6 inches in each revolution. Pre weighted sample of tablets was placed in the friabilator and were subjected to the 100 revolutions. Tablets were dusted using a soft muslin cloth and reweighed. The friability (F) is given by the formula.

$$F = \frac{W_{initial} - W_{final}}{W_{initial}} \times 100$$

Hardness [51]:

The tablet hardness is the force required to break a tablet in a diametric compression force. Erweka hardness tester (Erweka, Germany) was used in this study. This tester applies force to the tablet diametrically. The test was performed on six tablets and the average was calculated.

Water Absorption Ratio [51]:

A small piece of tissue paper folded twice is placed in a small petridish containing 6 ml of water. Put a tablet on the paper and the time required for complete wetting is measured. The wetted tablet is then reweighed. Water absorption ratio, R is determined by using following formula

R= 100 x Wa-Wb / Wb

Where, Wb is the weight of tablet before water absorption

Wa is the weight of tablet after water absorption

Uniformity of Dispersion [14]:

Keep the Two tablets in 100ml water and stir gently for 2 minutes. The dispersion is passed through 22 meshes. The tablets will consider passing the test if no residue remained on the screen.

Wetting Time [14]:

Five circular tissue papers of 10 cm diameter are placed in a petri dish with a 10 cm diameter. Ten millimeters of water containing Eosin, a water-soluble dye, is added to petri dish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as a wetting time.

Disintegration time:

Disintegration time is an important test in ODT technology since the tablet has to complete

disintegration within 1 min as per USP requirement. Tablet disintegration is measured using USP disintegration apparatus. A tablet is positioned in each tube and the basket rack is placed in a beaker of phosphate buffer at 37 ± 2 ˚C. The basket assembly is moved up and down the beaker and the apparatus is operated until no residue is left. The time taken to achieve zero residue is recorded. [53]

According to the European pharmacopoeia the fast disintegrating or Orodispersible tablets should disintegrate within 3 minutes without leaving any residue on the screen. However, it is difficult to assess the disintegration rate even in small amounts of water. Further the conventional test employs a volume of 900 ml of distilled water compared to the volume of saliva in humans, which is limited to a few ml. Thus, the disintegration rate obtained from conventional test does not appear to reflect the actual disintegration rate in human mouth. To overcome these problems, several new methods have been proposed. One of these methods uses a Charge Couple Device (CCD) camera or texture analyzer to evaluate the disintegration time of tablets. In another method, a modified DT apparatus is used. Here a wire basket of 3cm height and 2 cm diameter and mesh size of #10 is placed above a beaker containing 900 ml of simulated saliva. The basket is so positioned in the liquid that it contains only 6 ml of the liquid. The assembly is supported with a heater to maintain temperature at 37°C and a magnetic stirrer. DT is noted at 25 rpm. One of the simplest methods is to take 6ml of simulated saliva in a measuring cylinder and place the tablet in it. The liquid is neither shaken nor stirred and DT is noted. [52]

Dissolution test [54]:

USP apparatus 1 or 2 can be implemented for dissolution examinations. When apparatus type 1 (basket method) is used, some errors could occur due to the obstruction of basket pores by clog forming; therefore, in these cases, apparatus type 2 (paddle method) is used. The preferred rotation speed is 50 rpm for the dissolution test, but the rotation speed can be 100 rpm for the taste-masked ODTs. it should be kept in mind that a low paddle speed could create better discrimination between in vitro dissolution profiles. According to FDA, a minimum of 85% of the API in ODTs ought to be dissolved in 30 min to meet the requirement. Analytical methods such as UV-Vis spectroscopy and high-pressure liquid chromatography (HPLC) are generally used to measure the quantity of dissolved API

Table 3: List of Marketed products and Patented Technologies [41].

Patented Technology	Basis of Technology	Active Ingredient	Brand Name	Drug Release
Zydis	Lyophilization	Loratidine	Claritin reditab and Dimetapp quick dissolve	Dissolves in 2 to 10 sec.
Orasolv	Direct Compression	Paracetamol Zolmitriptan	Tempraquicklets, Zolmigrepimelt	Disintegrates in 5 to 45 sec
Durasolv	Direct Compression	Hyoscyamine Sulphate Zolmitriptan	NuLev,Zolmig ZMT	Disintegrates in 5-45 sec
Wowtab	Direct Compression	Famotidine	Gaster D	Disintegrates in 5-45 sec
Flashdose	Cotton candy process	Tramadol HCl	Relivia flash dose	Dissolves within 1 minute
Flashtab	Direct Compression	Ibuprofen	Nurofen Flash Tab	Dissolves within 1 minute
Quicksolv	Lyophilization	Cisapride Monohydrate Risperidone	Propulsidquicksolv Risperdal MTab	-----
Lyoc	Lyophilization	Phloroglucinol hydrate	SpasfonLyoc	-----

Ziplets Advatab	Direct Compression Microcaps and diffusecap CR technology	Ibuprofen Cetrizine Paracetamol	Cibalgina due fast Adva Tab cetrizine Adva Tab paracetamol	Disintegrates in less than 30 secs.
Oraquick	Micromask taste masking	Hyoscyamine sulphate ODT	Hyoscyamine sulfate ODT	-------

Table 4: Marketed Formulations along with Category [41]

API	Trade Name	Category
Piroxicam	Felden fast melt	NSAID
Loratidine	Claritin redi Tab	Antihistamine
Rizatriptan	Maxalt MLT	Migrane
Olanzapine	Zyprexia	Antipsychotic agent
Famotidine	Pepcid RPD	Antiulcer
Ondansetron	Zofran ODT	Anti-emetic
Zolmitriptan	Zoming-ZMT	Anti-migraine
Selegilline	Zeplar TM	Parkinson's disease
Acetaminophen	TempraQuiclets	Analgesic
Paracetamol	Febrectol	Anti- pyretic and analgesic
Nimesulide	Nimulid MDT	NSAID
Rofecoxib	Torrox MT	Used in treatment of osteoarthritis
Olanzapine	Olanexinstab	Antipsychotic agent
Diphenhydramine and Pseudoephedrine	Benadryl Fastmelt	Allergy, sinus pressure relief
Montelukast	Romilast	Anti-allergic drug
Cisapride monohydrate	PropulsidQuicksolv	Gastrointestinal prokinetic agent
Risperidone	Risperdal MTab	Schizophrenia
Ibuprofen	NurofenFlashTab)	NSAID
Paracetamol	TempraQuicklets	Anti- pyretic and analgesic
Zolmitriptan	ZolmigRepimelt	Anti-migraine
Ibuprofen	CibalginaDueFast	NSAID
Tramadol HCl	Relivia Flash dose	Analgesic
Hyoscyamine Sulfate	Hyoscyamine Sulfate ODT	Anti-ulcer

CONCLUSION:

Mouth dissolving tablets have better patient acceptance and offer improved biopharmaceutical properties, improved efficacy and better safety as compared with conventional oral dosage forms. By using new manufacturing technologies, many drugs can be formulated in the form of mouth dissolving tablets to provide the advantages of liquid medication in the form of solid preparation. The key to mouth dissolving tablets formulations is fast disintegration, dissolution, or melting in the mouth, and this can be achieved by producing the porous structure of the tablet matrix or adding superdisintegrant and/or effervescent excipients. Among all conventional technologies lyophilization technique is the most useful technique for the formulation of mouth dissolving tablets. In lyophilization technique we can formulate heat sensitive drugs and biologics with lower disintegration time where as in other techniques like heat moulding, spray drying requires high amount of temperature for the formulation of mouth dissolving tablets. Prescription ODT products initially were developed to overcome the difficulty in swallowing conventional tablets among pediatric, geriatric, and psychiatric patients with dysphagia. Today, ODTs are more widely available as OTC products for the treatment of allergies, cold, and flu symptoms. The target population has expanded to those who want convenient dosing anywhere, anytime, without water. The potential for such dosage forms is promising because of the availability of new technologies combined with strong market acceptance and patient demand. By paying close attention to advances in technologies, pharmaceutical companies can take advantage of

ODTs for product line extensions or for first to-market products. With continued development of new pharmaceutical excipients, one can expect the emergence of more novel technologies for ODTs in the days to come.

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