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ORODISPERSIBLE TABLETS: FORMULATION APPROACHES, EVALUATION PARAMETERS, AND RECENT INNOVATIONS

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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.

1. 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. 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. 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.

Today, ODTs are more widely available as OTC products for the management of many conditions such as allergies, cold, and flu symptoms. The presence of a highly porous surface in the tablet matrix is the key factor for rapid disintegration of ODT. To improve the porosity, volatile substances such as subliming agents can be used in tableting process, which sublimated from the formed tablet. Also freeze-drying technique is used to form a highly porous ODT. 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.

Orally disintegrating tablets are also called as orodispersible tablets, quick disintegrating tablets, mouth dissolving tablets, fast disintegrating tablets, fast dissolving tablets, rapid dissolving tablets, porous tablets, and rapimelts. However, of all the above terms, United States pharmacopoeia (USP) approved these dosage forms as ODTs. Recently, European Pharmacopoeia has used the term orodispersible tablet for tablets that disperses readily and within 3 min in mouth before swallowing.

1.1 Advantages of Orodispersible Tablets:

- Rapid disintegration of tablet results in quick dissolution and rapid absorption which provide rapid onset of action.
- Allows high drug loading.
- Alternative to liquid dosage form.
- Formulation is cleared from the esophagus especially in the supine position without lodging or sticking to it when swallowed, thus offering improved safety.
- Cost effective.
- No risk of choking.

- New business opportunities; line extension, exclusively of product promotion and patent life extension.
- 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.
- Convenient for administration and patient compliant for disabled, bedridden patients and for travelers and busy people who do not always have access to water.
- Good mouth feel property helps to change the perception of medication as bitter pill particularly in pediatric patients.

1.2 Disadvantages of Orodispersible Tablets:

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

1.3 Ideal Characteristics of Orodispersible Tablets:

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

1.4 Challenges In Formulation Of ODTS

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.

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:

- Layering the drug onto inert beads using a binder followed by coating with a taste-masking polymer.
- Granulating the drug and coating with a taste masking polymer.
- Spray drying the drug dispersed or dissolved in a polymeric solution to get taste-masked particles.
- Complexation by the use of inclusion in cyclodextrins.
- Psychological modulation of bitterness.
- Coacervation to form microencapsulated drug within a polymer.
- Formation of pellets by extrusion spheronization.

3. Sensitivity To Environmental Conditions: 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: 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: 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.

1.5 Drug Selection Criteria

The ideal characteristics of a drug for oral dispersible tablet include

- Ability to permeate the oral mucosa.
- At least partially non-ionized at the oral cavity pH.
- Have the ability to diffuse and partition into the epithelium of the upper GIT.
- Small to moderate molecular weight.
- Low dose drugs preferably less than 50 mg.
- Short half life and frequent dosing drugs are unsuitable for ODT.
- Drug should have good stability in saliva and water.
- Very bitter or unacceptable taste and odour drugs are unsuitable for ODT.

2. METHODS USED FOR PREPARATION OF ODTs:

2.1. Non – Patented Technologies:

2.1.1. Lyophilization/Freeze-Drying: In this process, produced products are porous in nature. The process in which from a solution the solvent is removed with additives forming structures or a suspension which is frozen is known as Lyophilization. Drugs that have been freeze-dried with additives provide an amorphous, glossy structure that makes the final product extremely lightweight and porous. In contact with the tongue, the tablet disintegrates quickly and dissolves, and the drug is released when the lyophilized unit melts. However, this technique decreased mechanical strength and stability at elevated humidity and temperature.

Excipients such polymers (to provide the tablets strength and stiffness, such as dextrin, gelatin and alginates); polysaccharides (to improve palatability, crystallinity and hardness of the matrix, such as sorbitol and mannitol); anti-collapse excipients (to stop the shrinking of the product in its packaging throughout production or storage, such as glycine); flocculating agents (to ensure uniform drug particle dispersion, such as gum acacia); preservatives (to protect microbiological development, like methyl parabens); penetration enhancer (to increase permeation of transmucosal like Sodium Lauryl Sulphate); pH modifier (for stability like citric acid); Water is added for the creation of pores, while flavours and sweeteners help patients to comply with treatment are commonly used in ODTs produced by the lyophilization method

2.1.2. Tablet Moulding: Typically, water-soluble substances are found in moulded tablets, resulting in complete and rapid dissolution. The various processes for moulding tablets are as follows:

Compression Moulding: In This technique the powder combinations are wetted with hydro-alcoholic solvent and pressed into a wetted mass with the help of mould plates. Tablet triturates are prepared by removing the solvent by air drying. The compactness of the prepared tablets are less in comparison to compressed one, and they dissolve more quickly due to their porous structure.

Heat-Moulding: This process involves creating a liquefied substance that contains the evenly distributed drug. For preparing the tablet, agar solution is used as a binding agent here; blister packing is used for moulding. Initially a suspension consisting of sugar, agar and drug is prepared. After that, the resulting mixture is poured to the blister packaging, where it is then dried under vacuum at a temperature of about 30°C.

Moulding by Vacuum Evaporation without Lyophilization: Here, at first the API and other additives should be mixed, and then the mixture is poured in a matrix of required extent, form a solidified matrix by freezing and at last at a temperature, vacuum drying is done between its equilibrium freezing temperature and its collapse temperature. As a result, a matrix which is partially collapsed is created. The difference between this process and the technique of lyophilization is that the previous involves the controlled evaporation from a solid of free solvent which is unbound via the liquid phase to a gas. The later approach involves sublimation. Opposite to lyophilization, vacuum drying assists in densifying the matrix, which raises the product's mechanical strength.

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2.1.3. Direct Compression *(DC):* Due to the few processing stages, low production costs, and ability to handle high doses, this method makes it simple to formulate ODTs. The final weight of a tablet can simply be more than that of another technique of manufacture. The effects of the disintegrant, water-soluble excipients and effervescing agents can be used alone or in combination to determine how easily directly compressed tablets dissolve. The hardness and size of the tablet have a big impact on how well it disintegrates. The disintegration properties can be enhanced by moderate or smaller size of tablet, minimum physical resistance and low hardness. Selecting an appropriate and ideal concentration of disintegrant is essential for ensuring rapid disintegration as well as rapid dissolving rates. In order to further improve dissolution or disintegration capabilities, water soluble excipients or

effervescent agents may be used. Due to the formulation's combination of swelling and water absorption, super disintegrants offer fast disintegration.

2.2 Mechanism of Action of Super Disintegrants:

The tablet breaks to primary particles by one or more of the mechanisms listed below:-

- ✓ By Capillary Action
- ✓ By Swelling
- ✓ Because Of Heat Of Wetting
- ✓ Due To Release Of Gases
- ✓ By Enzymatic Action
- ✓ Due To Disintegrating Particle/Particle Repulsive Forces
- ✓ Due To Deformation

A. By Capillary Action: Disintegration by capillary action is always the first step. When we put the tablet into suitable aqueous medium, the medium penetrates into the tablet and replaces the air adsorbed on the particles, which weakens the intermolecular bond and breaks the tablet into fine particles. Water uptake by tablet depends upon hydrophilicity of the drug /excipient and on tableting conditions. For these types of disintegrants, maintenance of porous structure and low interfacial tension towards aqueous fluid is necessary which helps in disintegration by creating a hydrophilic network around the drug particles.

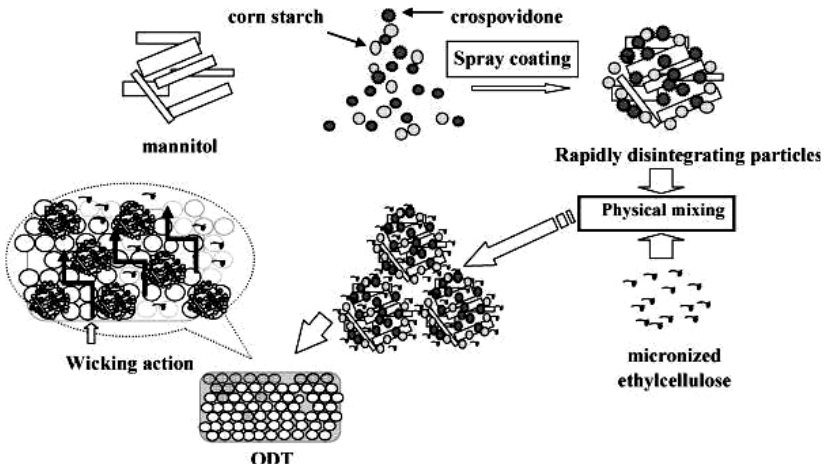

Figure 1: Disintegration Through Wicking Action.

B. By Swelling: Perhaps the most widely accepted general mechanism of action for tablet disintegration is swelling. Tablets with high porosity show poor disintegration due to lack of adequate swelling force. On the other hand, sufficient swelling force is exerted in the tablet

with low porosity. It is worthwhile to note that if the packing fraction is very high, fluid is unable to penetrate in the tablet and disintegration is again slows down.

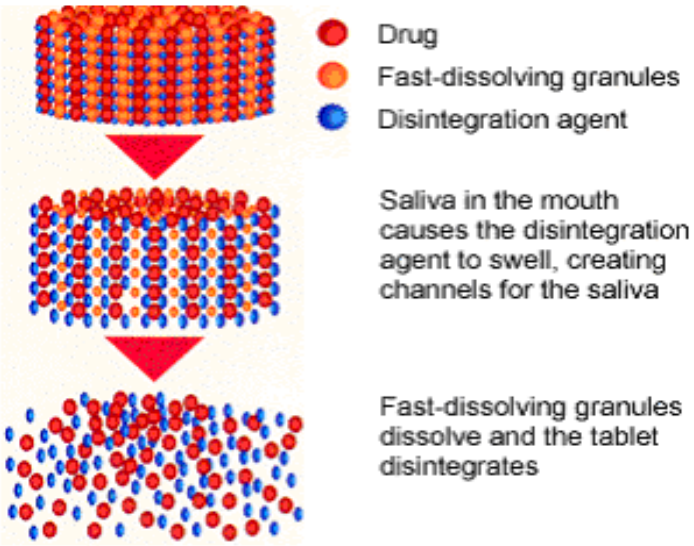

Figure 2: Disintegration Through Swelling Mechanism.

C. Because Of Heat of Wetting (Air Expansion): When disintegrants with exothermic properties gets wetted, localized stress is generated due to capillary air expansion, which helps in disintegration of tablet. This explanation, however, is limited to only a few types of disintegrants and can not describe the action of most modern disintegrating agents.

D. Due To Release of Gases: Carbon dioxide released within tablets on wetting due to interaction between bicarbonate and carbonate with citric acid or tartaric acid. The tablet disintegrates due to generation of pressure within the tablet. This effervescent mixture is used when pharmacist needs to formulate very rapidly dissolving tablets or fast disintegrating tablet. As these disintegrants are highly sensitive to small changes in humidity level and temperature, strict control of environment is required during manufacturing of the tablets. The effervescent blend is either added immediately prior to compression or can be added in to two separate fraction of formulation.

E. By Enzymatic Reaction: Here, enzymes present in the body act as disintegrants. These enzymes destroy the binding action of binder and helps in disintegration. Actually due to swelling, pressure exerted in the outer direction or radial direction, it causes tablet to burst or the accelerated absorption of water leading to an enormous increase in the volume of granules to promote disintegration.

F. Due To Disintegrating Particle/Particle Repulsive Forces: Another mechanism of disintegration attempts to explain the swelling of tablet made with 'non---swellable' disintegrants. Guyot--- Hermann has proposed a particle repulsion theory based on the observation that non-swelling particle also cause disintegration of tablets. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it. Researchers found that repulsion is secondary to wicking.

G. Due To Deformation: Hess had proved that during tablet compression, disintegranted particles get deformed and these deformed particles get into their normal structure when they come in contact with aqueous media
or water.

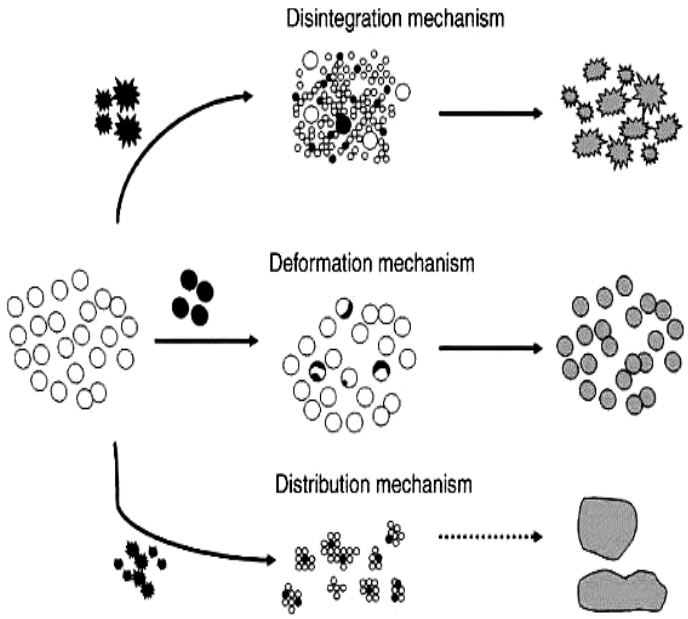

Figure 3: Disintegration Through Deformation Mechanism.

2.3 Sugar Based Excipients

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.

Spray-Drying: In this technique the organic solvent evaporated resulting porous tiny particles. Here croscarmellose sodium or sodium starch glycolate are choice of super-disintegrant, mannitol as diluent, and both hydrolysed and non-hydrolysed gelatin is used as the supporting matrix. By adding alkali or acidic compounds like acidic acid and sodium bicarbonate respectively, dissolution and disintegration were accelerated even further. The porous powder produced by this formulation method has a disintegration time of 20 seconds or less.

Cotton Candy Process: It is so called as it has a unique mechanism of spinning to prepare a crystalline structure that looks like a floss and which is similar to cotton candy. In order to form a matrix containing polysaccharides or saccharides, flash melting as well as spinning are done simultaneously under the cotton candy method. Partial crystallization of the matrix leads to enhance its fluidity. After milling and blending this candy floss matrix with the active ingredients and additives, it prepares ODTs by compressing them.

Sublimation: High porosity ODTs have been created using sublimation. Conventional tablets sometimes fail to dissolve quickly despite having highly water-soluble components due of their poor porosity. During the tableting process, the volatile components can increase the porosity through sublimation. The volatile components and other excipients are compressed into tablets before being subjected to a sublimation process; as a result a porous matrix is formed. For this, inert solid substances with high volatility, such as urea, urethene, naphthalene, hexamethylene tetramine, benzoic acid, camphor, and ammonium bicarbonate, have been like cyclohexane and benzene were also proposed. Created MDTs utilizing camphor, a volatile substance derived from compacted tablets composed of a camphor-mannitol blend. Camphor was made into tablets, and then they were evaporated for 30 minutes at 80°C in a vacuum.

- **Mass-Extrusion:** With this innovation, the active mixture is made soft using a water-soluble mixture of carbinol and PEG, and the relaxed mass is ejected through an extruder to urge a hollow, rounded extrude that is then cut into even pieces using a warmed edge to prepare tablets. In order to disguise the flavour of bitter pharmaceutical granules, this procedure can also be utilized.
- **Nanonization:** A recently created technique termed as Nanomelt, decreases drug particle size into nanoscale by using a revolutionary wet-milling method. Adsorption on specific stabilizers on the surface ensures that the drug nanocrystals are protected from clumping

together, allowing for their seamless incorporation into MDTs. Poorly water-soluble drugs get great benefit by this method. The rapid dissolution/disintegration of nanoparticles leads to enhanced absorption, consequently improving bioavailability and allowing for dosage reduction, as well as the technology's cost-effective manufacturing procedure, are additional benefits.

- **Melt Granulation:** The hydrophilic PEG-6-stearate is used as waxy binder to prepare the MDTs. It has HLB value of 9 (which indicates balanced hydrophilic-lipophilic profile) and melting point 33-370C. Not only it functions as a binder but also strengthens the hardness of the tablets, but it aids in tablet disintegration by swiftly melting and rapidly solubilizing without leaving any residue in mouth. The molten form of super polystate is used to create granules in the formulation of ODTs.
- **Fast Dissolving Films:** Here the drug and other ingredients are dissolved in organic solvent and a hydrophilic polymer which forms a film (Hydroxypropyl methylcellulose, carboxy methylcellulose, sodium alginate etc.) is mixed and the solvent is allowed to evaporate for the formation of the film. When using pungent drugs, coated microparticles or resin adsorbate of the drug may be added to the film. After administering in the mouth, the drug is released as a suspension or solution in which the film readily dissolves. This system's advantages include rapid delivery of drugs, disintegration in 5 seconds, and flavoured after taste.

Three-dimensional Printing (3DP): It is a type of rapid prototyping (RP) technology. With the use of liquid binding materials and powder processing, prototypes are built up from specified layers. Drug delivery device (DDD) which contained loose particles is fast dissolving, which is created by the three-dimensional printing (3DP) method. The 3DP system automatically prepared the DDD carrying -aided design models.

2.4 Patented Technologies

Zydis Technology: This technique includes the physical entrapment of the drug inside a polymer and saccharide matrix. Alginates, polyvinyl alcohol, polyvinyl pyrrolidine, hydrolyzed dextran, partially hydrolyzed gelatin, dextrin, and these mixes are the most often used polymers. The process entails combining pre-prepared components, which are then dispersed or dissolved prior they are subjected to freezing in a liquid nitrogen environment. To produce porous wafers, the frozen solvent is allowed to sublime. The drug used to prepare the MDT is Loratidine.

Lyoc: PHARMALYOC holds the patent for this technology. The blister cavities are filled with a prepared oil-in-water emulsion, which is then freeze-dried. Non-homogeneity is prevented by enhancing viscosity with inert filler before allowing sediment to settle out while freeze-drying. Content with high filler makes tablets less porous, which slows down disintegration. The drug used to prepare the MDT is Phloroglucinol Hydrate.

Quick Solv: The Janssen Pharmaceutical Company holds the patent for the invention. Two solvents are combined to form a matrix, which gets disintegrated rapidly. In this method, Water is used to dissolve the matrix components, and the dispersion or solution is then refrigerated.The water is then extracted from the matrix by applying an excessive amount of alcohol, which causes the matrix to dry. Thus, the resultant product is uniformly porous as well as strong enough to handle. The drugs used to prepare the MDT are Cisapride monohydrate and Risperidone.

Flash tab Technology: Ethypharm France holds the patent for this technology. This process involves compressing the excipients into tablets after either dry granulation or wet granulation of the drug and excipients. Excipients used in this technique fall into two different categories. Carboxymethylcellulose and reticulated polyvinyl pyrrolidone are examples of disintegrating agents. Starch, carboxymethylated starch, Carboxy methylcellulose, microcrystalline cellulose etc. are examples of swelling agents. Physical resistance is adequate for these tablets. These tablets disintegrate in less than a minute. The drug used to prepare the MDT is Ibuprofen.

Ceform Technology: Fuisz holds the patent for this technology. The active drug's microspheres are prepared using this technology. The drug material is put alone or in combination with other pharmaceutical excipients and components in a quickly spinning machine which is constructed very precisely. The centrifugal force propels the dry drug mixture rapidly via hot openings. The heat created by precisely regulated temperature causes the drug blend to liquefy to form a spherical shape, with no effect on the drug's stability. Tablets are created by compressing the resultant microspheres. When drugs and excipients are processed together, a unique microenvironment is created that allows the ingredients characteristics, and enhancing solubility and stability.

Shear form Technology: Fuisz holds the patent for this technology. "Floss" is a shearform matrix which is prepared by this method. The feedstock which is prepared with sugar carrier

is processed using flash heat. Here, sugar is subjected at the same time to both temperature gradient and centrifugal force. This leads to rise in the mass's temperature which in turn creates a flow situation internally that allows moving relatively to the mass for some of the sugar. The rotating head that lets the flowing mass exit by flinging the floss. The floss which is created has a texture of amorphous nature. To create a flow consistency and make it easier to mix, it is further diced using a variety of methods and also recrystallized. The recrystallized matrix, active component, and additional excipients are then mixed, and the mixture is then pressed into tablets.

Flash dose Technology : Fuisz holds the patent for this technology. To disguise the unpleasant taste of the medicine, this system combines both the Shearform and Ceform technologies. Excipients (sugars of crystalline nature), either single or in combination with drugs, are combined to form a sugar-based matrix known as "Floss" is used. The first commercial product created using this technique was released by Biovail Corporation as a new version of Ibuprofen called Nurofen meltlet, which dissolves in the mouth.

Orasolv Technology: CIMA Labs has a patent on this invention. To create the MDTs, disintegrating agents of effervescent nature undergo compression at low pressure. The fizzing feeling produces positive organoleptic characteristics by the release of carbon dioxide from tablets. 20–25% of the weight of tablet is the typical concentration of the effervescent mixture used.

Durasolv Technology: CIMA Labs holds the patent for this invention. In this technology, Conventional tableting equipments are used to manufacture the tablets. Mannitol, lactose, sucrose and sorbitol are non-direct compressible fillers that have the advantage of dissolution rapidly while avoiding the granular texture that is typically found in sugar of direct compressibility. The obtained tablets can be packed into blisters or bottles as they are very strong. The drugs used to manufacture the MDT are Hyoscyamine Sulphate and Zolmitriptan. Because the tablets are made with a minimal force of compression, they are fragile and soft. This led to the creation of Paksolv, modified packaging designed to prevent tablet breakage during storage and transportation. By using this Paksolv which is a blister package of dome-shaped, Prevention occurs of the vertical movement of the tablet. Paksolv offers packaging that is light, moisture, and child-resistant. The drugs used to manufacture the MDT are Paracetamol and Zolmitriptan.

WOW tab Technology: Yamanouchi Pharma Tech. Inc. patented this tehnology. The name WOW stands for "without water." This methodology makes use of traditional granulation and

tableting techniques to create MDTs using saccharides with low such as Lactose, Glucose, Sucrose and high moldability such as Sorbitol, Maltose, Oligosaccharides, and Manitol. Due to lack of desired properties of any one moldability saccharide alone, combination of both saccharides is used to prepare the MDT in this technique. With this approach, combined granulated saccharide as a binder, compressed into tablets, and then treated with moisture. Thus, the resulting tablets showed acceptable hardness and very quick disintegration. The drug used to manufacture the MDT is Famotidine.

Ora quick: The pharmaceutical company K.V.S. has the patent on this invention. It makes use of the microsphere of taste masking technique known as micromask, which offers an improved tongue feel, high mechanical strength, and rapid product dissolution/disintegration. As part of this procedure, microparticles are created in the shape of a protective matrix for the drug that has the necessary mechanical strength to be compressed. This method is excellent for heat sensetive drugs because of the decreased manufacturing temperatures. For dissolving oraquick it takes a few seconds.

2.5 Excipients Used To Prepare ODTS:

- **Super-Disintegrants:** Pregelatinized Starch, Modified Corn Starch, Sodium Starch Glycollate, Crospovidone, Calcium Carboxymethylcellulose and Microcrystalline Cellulose. SSG has better flowability than CCS. The fibrous substance crospovidone has excellent compactability.
- **Flavoring Agents:** Peppermint flavor, flavored oil and oil like anise, clove, thyme oil, peppermint, bay, eucalyptus, citrus, vanilla, bitter almonds, and fruit essences.
- **Fillers:** Pregelatinized starch, Sorbitol, aluminium hydroxide, Mannitol, magnesium carbonate, calcium carbonate, magnesium trisilicate, calcium phosphate, and xylitol are all directly compressible spray-dried ingredients.
- **Surfactants:** Sodium dodecyl sulfate, Tweens, SLS, Spans, Polyoxyethylene stearate etc are the examples of surfactants used in ODTs.
- **Binding Agents:** PVA, HPMC, PVP etc are the examples of Binding agents used in ODTs.
- **Lubricants:** Zinc state, Stearic acid, calcium state, talc, Magnesium stearate, Magnesium lauryl sulfate, liquid paraffin etc are the examples of lubricants used to prepare ODTs.
- **Coloring Agent:** Amaranth, Sunset yellow etc. are the examples of coloring agents used to prepare ODTs.

3. PRE-FORMULATION STUDIES OF ODTs

The term "pre-formulation study" refers to pharmaceutical and analytical research done prior to and in support of formulation development activities of the drug substance's dosage form. Pharmaceutical excipients with drug combination are added to the dosage form which provides information that is necessary to define about drug substances nature. Therefore, on the drug sample that was collected, the following pre-formulation investigations were carried out:

Angle of Repose (θ): It indicates friction forces of the setting powder. Between the horizontal plane and powder pile surface a greatest angle is formed which is characterized by the angle of repose. A funnel at a specific height was set up on the stand, and through which the flow of powder mixture was allowed. The height and radius of the created hill of powder were then measured to determine the angle of repose.

$$\tan\theta = h / r$$

$$\text{Or, } \theta = \tan^{-1}(h / r)$$

Where, θ = Angle of Repose; h = Pile Height; r = Heap Radius (Powder occupied plane surface).

Bulk Density (ρb): It is the mass (M) to bulk volume (Vb) ratio. For measuring it, a person should pour the pre-sieved powder mix into a graduated cylinder and take the weight. The measured volume is known as Bulk Volume. The unit used to express the bulk density is g/ml. To calculate the Bulk Density a person needs to put the above-mentioned measurements into the equation:

$$\rho b = M / Vb$$

Where, M = Powder Mass, Vb= Powder Bulk Volume

Tapped Density (ρt): It is the mass (M) to tapped volume (Vt) ratio. For measuring the tapped density, a person should pour the pre-sieved powder mix into a graduated cylinder and place it on a mechanical tapping apparatus. After placing the measuring cylinder on the apparatus, start the tapping apparatus and let it run until no changes in the volume noticed. The unit used to express the tapped density is g/ml. The calculation of tapped density is done by the equation:

ρt = M/Vt

Where, M = Powder Mass, Vt = Powder Tapped Volume.

Carr's Index: By this a person comes to know about the flowability of powder. The formula for calculating it is:

%Compressibility = [(Tapped Density - Bulk Density) / Tapped Density] × 100

Hausner Ratio: Measurement of the flow property of the drug-excipients mixed powder. The formula for calculating Hausner Ratio is:

Hausner Ratio = Tapped Density / Bulk Density.

Porosity (€): Experimentation can confirm the expectations that porosity is an excellent indicator of how liquids will penetrate the tablet matrix. In a study on the development of tablet formulations, tablet volume and total weight were used to calculate the porosity values. The equation helps to calculate the porosity is:

% (€) = [(1 - (W/Vρ)) x 100]

Where, W = Tablet weight, V = Tablet volume, ρ = Powder True density

4. EVALUATION STUDIES FOR ODTs:

After preparing tablets some tests should be done to understand the activity of the tablet. These tests or studies are known as Evaluation studies.

Overall Appearance: The overall appearance of a tablet is the outlook of the tablet which helps in customer acceptance. It includes the Shape, Size, Odour, Colour, Surface texture etc. of the tablets**.**

Thickness of Tablet: It is one of the very important evaluation studies as by this study a person can presume whether the amount of the filler was sufficient or not during the tablet preparation. Generally, ten random tablets are taken to measure the thickness and their average is calculated. Vernier Calipers can be used to measure the thickness of a tablet. The unit used to express the thickness of a tablet is mm.

Measurement of Tensile strength of Tablets: It is nothing but to determine how hard the tablet is. It can be measured by applying the required force to break down the same.

Monsanto Hardness Tester is used to measure tablet hardness. The unit used to determine the Tensile Strength is Kg/cm2. It can be calculated by the following formula:

$T = 2F / \pi dt$

Where, F = Crushing load, d = diameter, t = thickness37In spite of being a widely accepted method, this method is not used for the tablets made by lyophilization technique38. This test is generally done for tablets which are made by direct compression method or by moulding method. The tensile strength should be less for Orodispersible Tablets to ensure less disintegration time.

Weight Variation: After taking random 20 tablets, individually their weights are taken on the weighing balance machine and the average weight is determined. By this method, uniformity of drug content can be predicted.

Friability: According to Pharmacopoeia a friability test should be done for 4 minutes at 25 rpm (100 rotations). The maximum acceptance limit for weight loss is 1% of its original weight. After tumbling, if any tablet gets cracked, chipped or broken, the whole sample gets disqualified from the test41. The test is not performed for tablets made with the Lyophilization technique or Flashdose Technique. But for tablets made with the direct compression method and moulding method, this test is most recommended. The purpose of this test is to make sure the tablet has sufficient mechanical strength to endure shipping-related abrasion38. The percentage of Friability can be determined by this equation:

$\%\ Friability = \{(W1 - W2) / W1\} \times 100$

Where, W1 = Initial weight, W2 = Final weight

Moisture Uptake Study: A lot of hydrophilic additives with least amount of hardness is contained in MDTs, which collectively increases their sensitivity to moisture absorption. Special care must be taken when storing and packaging these forms of dosage to safeguard their structural integrity and surface texture. Therefore, it is strongly recommended to perform moisture uptake study for MDTs. Ten tablets can be used for the test, along with calcium chloride, and they can be kept in a desiccator for a day at room temperature. After weighing keep it in room temperature for two weeks at 75% relative humidity. The weight gain percentage is calculated after reweighing the tablets. A product needs a dedicated dehumidified room for manufacture and packaging if its tendency to absorb moisture is high.

For packaging, it is best to utilize materials with a high degree of moisture resistance. It is strongly advised to use an appropriate amount of adsorbent in HDPE bottle pack with the least amount of head space possible to ensure the longevity of the product throughout its shelf life.

Tablet Porosity Measurement: Tablet porosity is measured by using mercury penetration porosimeter. It is an assessment in the formulation by the degree of water which leads to fast disintegration. Phenomenon of capillary rise where more pressure is needed to form a liquid of non-wetting nature is based on by this capillary. In this test, the surface tension is 0.486 N/m between the tablet and mercury and the contact angle between the two is maintained at 140°. This method is effective for measuring pores between 0.06 μm to 3.60 μm39 by the following equation:

$$\Delta P = -(2\gamma/r)cos\theta$$

Where, γ = Surface tension, r = Perpendicular radius, θ = angle between capillary walls and liquid. This equation is known as the Washburn equation.

If the calculation is not possible by the above-mentioned equation due to the variation of the pore size, the below mentioned equation can be used:

$$\varepsilon = 1 - m/(\rho t V)$$

Where, ρt = True density, m = Tablet weight, and V = Tablet volume.

Wetting Time and Water Absorption Ratio: A double folded tissue paper is placed in a petri dish containing 6 ml water. A pre-weighed tablet is placed on that and note the time for complete wetting which is the wetting time. Then, after weighing that wetted tablet, the ratio of water absorption is calculated by using this formula:

$$R = \{(Wa - Wb) / Wb\}x100$$

Where, Wb = Tablet weight before water absorption, Wa = Tablet weight after water absorption.

Disintegration Test: It is performed to determine whether the product (Here MDT) is disintegrating within the time which is prescribed after placing it in a medium of liquid or not. The tests should be done with 6 tablets with the help of the apparatus specified in Indian

Pharmacopoeia. As the liquid media distilled water should be used at 37±2°C temperature41. After fulfilling all the criteria, the disintegration time should be noted in seconds using a stopwatch. The maximum time should be 180 seconds for disintegrating a mouth-dissolving tablet.

Dissolution Test: To evaluate ODTs in vitro, the common technique of dissolution can be used. Preliminary in-vitro investigations can be used to better simulate in vivo environments by using the dissolving conditions for the reference mentioned drugs that are accessible in USP. To understand their*in-vivo* effectiveness and pharmacological equivalence, multimedia dissolving tests in different pH levels of a variety of buffer solutions, such as pH 1.2, 4.5 and 6.8 buffers should be conducted, with a speed of 50 rpm, USP apparatus 2 (paddle type) and an acceptable dissolving media volume for maintaining sink condition. When employing USP prescription conditions, MDTs often dissolve relatively quickly, and in these circumstances, the dosage forms act nearly similarly. Therefore, reduced paddle speeds can be used to develop profiles and improve during the developing stage. There is a chance that a pile will form at the dissolution vessel in the bottom part in the case of tablets that are close to or heavier than one gram and consist of reasonably dense insoluble particles. Increasing the paddle speed to 75 rpm can fix this problem.

In-vitro dispersion Time: Tablets containing solid dispersion formulations are evaluated using an *in-vitro* dispersion study. Solid dispersion technique improved the solubility and dissolution rates of hydrophobic drugs43. For this test three tablets from each batch are taken and individually dropped into 50 ml Sorenson's buffer pH 6.8 and measurement of *in-vitro* dispersion time is done.

Stability Study: The ICH recommendations for accelerated studies specify that the tablets which fast dissolves is kept in specific conditions for a certain duration of time after being packaged, i.e. at 37±1°C, 40±1° and 50±1°C, with a RH of 75%±5%. Then the removal of tablets and their physicochemical properties (like hardness, friability, visual flaws disintegration, and so on) and content of drug were examined after 15 days. First order equation is employed to determine the degradation kinetics. The shelf life at 25°C is calculated using accelerated stability data displayed with the Arrhenius equation.

5. FUTURE PERSPECTIVE

Despite the wide range of commercial medicines available, there are still numerous areas where MDT formulations might be strengthened. Despite today's highly developed MDT technology, it can still be difficult to formulate hydrophobic drugs, particularly when the dosage is high. Incorporating greater quantities of hydrophobic medications without compromising their ability to dissolve quickly is now possible thanks to a novel technique. Scientists should now eventually work on creating MDTs with controlled release characteristics. It would be a significant advancement in the MDT technique if one MDT could deliver medications having short half-lives lasting 12–24 hours. The development of efficient taste-masking qualities will lead to the invention of novel innovations in the future. Drugs with bitter tastes are frequently coated, however, this raises the overall finished formulation volume. Therefore, with ongoing advancements, one can anticipate the development of more unique techniques for MDTs in the days ahead. It is anticipated that in the near future, these fast-dissolving tablets would likely replace a significant portion of conventional products due to their exceptional advantages.

6. 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.

7. REFERENCES

1. Abd Elbary, A., Ali, A. A., & Aboud, H. M. *Enhanced dissolution of meloxicam from orodispersible tablets prepared by different methods*. Bulletin of Faculty of Pharmacy, Cairo University, *50(2)*: 89-97, (2012).
2. Elkhodairy, K. A., Hassan, M. A., & Afifi, S. A. *Formulation and optimization of orodispersible tablets of flutamide*. Saudi Pharmaceutical Journal, *22(1):* 53-61, (2014).
3. Puttewar, T. Y., Kshirsagar, M. D., Chandewar, A. V., &Chikhale, R. V. *Formulation and evaluation of orodispersible tablet of taste masked doxylamine succinate using ion exchange resin.* Journal of King Saud University-Science, *22(4):* 229-240, (2010).
4. Hirani, J. J., Rathod, D. A., &Vadalia, K. R. *Orally disintegrating tablets: a review*. Tropical journal of pharmaceutical research, *8(2)*: (2009)
5. Bandari, S., Mittapalli, R. K., &Gannu, R. *Orodispersible tablets: An overview.* Asian Journal of Pharmaceutics (AJP), *2(1)*: 2-11, (2008)
6. Jeevanandham, S., Dhachinamoorthi, D., Sekhar, K. C., Muthukumaran, M., Sriram, N., &Joysaruby, J. *Formulation and evaluation of naproxen sodium orodispersible tablets "A sublimation technique*. Asian Journal of Pharmaceutics (AJP), *4(1):* 48-51, (2010)
7. Kumar, R., Patil, S., Patil, M. B., Patil, S. R., &Paschapur, M. S. *Formulation evaluation of mouth dissolving tablets of fenofibrate using sublimation technique.* Int J Chem Tech Res, *1(4):* 840-50, (2009)
8. Kumar, R., Patil, M. B., Patil, S. R., Paschapur, M. S., & Mahalaxmi, R. (2009). *Development and characterization of orodispersible tablets of aceclofenac by sublimation technique.* International Journal of PharmTech Research, *1(2)*: 210-214, (2009)
9. Corveleyn, S., & Remon, J. P. *Formulation and production of rapidly disintegrating tablets by lyophilisation using hydrochlorothiazide as a model drug.* International Journal of Pharmaceutics, *152(2):* 215-225, (1997).

10. Shoukri, R. A., Ahmed, I. S., & Shamma, R. N. *In vitro and in vivo evaluation of nimesulide lyophilized orally disintegrating tablets.* European Journal of Pharmaceutics and Biopharmaceutics, *73(1)*: 162-171, (2009)
11. Puttewar, T. Y., Kshirsagar, M. D., Chandewar, A. V., &Chikhale, R. V. *Formulation and evaluation of orodispersible tablet of taste masked doxylamine succinate using ion exchange resin.* Journal of King Saud University-Science, *22(4):* 229-240, (2010).
12. Shukla, D., Chakraborty, S., Singh, S., & Mishra, B. *Mouth dissolving tablets II: An overview of evaluation techniques.* Scientia Pharmaceutica, *77(2)*: 327-342, (2009)
13. Shukla, D., Chakraborty, S., Singh, S., & Mishra, B. *Mouth dissolving tablets I: An overview of formulation technology.* Scientia Pharmaceutica, *77(2):* 309-326, (2009).
14. Arora, P., & Sethi, V. A. *Orodispersible tablets: A comprehensive review*. Int J Res Dev Pharm Life Sci, *2(2)*: 270-84, (2013).
15. Chang, R. K., Guo, X., Burnside, B. A., & Couch, R. A. *Fast-dissolving tablets*. Pharmaceutical technology, *24(6):* 52-58, (2000).
16. Reddy, L. H., & Ghosh, B. *Fast dissolving drug delivery systems: A review of the literature*. Indian journal of pharmaceutical sciences, *64(4)*, 331-336, (2002).
17. Roy, A. *Orodispersible tablets: a review*. Asian J Pharm Clin Res, *9(1):* 19-26, (2016).
18. Beri, C., & Sacher, I. *Development of fast disintegration tablets as oral drug delivery system-A review.* Indian J. Pharm, *1(3):* 80-99, (2013).
19. Hannan, P. A., Khan, J. A., Khan, A., & Safiullah, S. *Oral dispersible system: A new approach in drug delivery system.* Indian journal of pharmaceutical sciences, *78(1):* 2-7, (2016).
20. Swarbrick J, Encyclopedia of pharmaceutical technology. New York, USA: Informa Healthcare Inc. third edn, Vol 1; pp 1104 –1114, (2007).