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A Review on Orally Disintegrating Tablets

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K.Shobana

Department of Pharmaceutical Science, Jaya College of Pharmacy, Chennai, Tamil Nadu, India.

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ABSTRACT

Orally disintegrating tablets (ODTs) rapidly disintegrate or dissolve in the oral cavity without the use of water. Demand for ODTs is increasing, and the field has been becoming increasingly important in the global pharmaceutical market. It is reported that ODTs have several advantages over other conventional tablets. Since some of them are absorbed from the mouth, pharynx, and esophagus as the saliva passes down into the stomach, and so the bioavailability of the drug improves significantly. They are extremely important in prescription and over-the-counter medications because they can improve patient compliance. Furthermore, the immediate release property of ODTs makes them a popular oral dosage form in patients with swallowing challenges, children, and in cases where there is a need for rapid onset of action. The current review article explains the advantages, limitations, components, manufacturing procedures, patented technologies and assessment tests of ODTs.

INTRODUCTION

There has been an increase in demand for more patient-friendly dosage forms during the last decade. Pharmaceutical technologists have developed a novel oral dosage form called as Orally Disintegrating Tablets (ODTs) that dissolve fast in saliva, usually in a matter of seconds, without the requirement to consume it with water. The rate of drug dissolution and absorption, as well as the beginning of clinical action and drug bioavailability, may be much faster with ODTs than with traditional dosage forms. Even though chewable pills are available in the market but they are not the same as the new ODTs. Patients who find difficulty in chewing can also benefit from these new ODTs.

The ODTs technology, which allows tablets to dissolve or disintegrate in the oral cavity without the use of extra water, has received a lot of attention. Even when inserted in the mouth with limited bio-fluid, ODTs are enabled for fast solid breakdown or dissolving into a suspension or solution form. Orally disintegrating tablets are also known as orodispersible tablets, quick disintegrating tablets, fast disintegrating tablets, fast or rapid dissolving tablets, porous tablets, mouth dissolving tablets, and rapimelts. Excipients used in ODT technology are usually hydrophilic in nature and can be chosen based on the physicochemical qualities of the medication, such as hydrophilicity or hydrophobicity. If the active pharmaceutical ingredient is hydrophobic, the dosage form is referred to as a disintegrating tablet, whereas if it is hydrophilic, the dosage form is referred to as a quick-dissolving tablet.

The Food and Drug Administration (FDA) defines the ODT formulation as "a solid dosage form containing medical chemicals that disintegrates fast, usually within a matter of seconds when placed upon the tongue." Regulatory agencies have also approved a variety of medications for ODT formulations. In the guidance for the industry document “Size, Shape, and Other Physical Attributes of Generic Tablets and Capsules” published by CDER, US FDA, it is recommended that drug manufacturers develop quality target product profiles (QTPPs) for drug candidates. For ODTs, parameters such as disintegration time and tablet size are key components of QTPPs. The purpose of this article is to highlight the advantages, limitations, components, manufacturing procedures, patented technologies and assessment tests of ODTs.

ORALLY DISINTEGRATING DOSAGE FORMS (ODDF)

Orally Disintegrating Dosage Forms (ODDF) evolved from a desire to give patients with a

more traditional method of taking their medication. Surprisingly, the demand for ODDFs has skyrocketed in the last decade, especially among geriatric and pediatric patients who have trouble in swallowing traditional pills and capsules. As a result of this difficulty, they do not follow the prescription and this result in a high rate of unsuccessful therapy. Fast dissolve, rapid dissolve, rapid melt, and quick dispersible tablets are terms used to describe a new oral disintegrating dosage form technology. All these dosage forms, however, serve the same purpose and have the same concept.

PRINCIPLE OF ORALLY DISINTEGRATING TABLETS

The rapid disintegration of these tablets is due to the rapid entry of water into the tablet matrix, which results in a porous structure and rapid disintegration. As a result, optimizing the porosity structure of the tablet matrix by including the suitable disintegrating agent and using highly water-soluble excipients in the formulation are the primary approaches to developing ODTs.

Sudden episodes of coughing and repeated emesis make ingesting conventional solid dosage forms challenging in conditions like motion sickness. In such cases, orally disintegrating dosage forms can be an efficient alternate way of medication delivery. When these dosage forms are placed in the mouth, they rapidly disintegrate, releasing the medicine, which dissolves or disperses in the saliva. As the saliva moves down, the medication may be absorbed from the pharynx and esophagus, as well as other parts of the GIT. Bioavailability is substantially higher in these circumstances than with traditional tablet dosing forms.

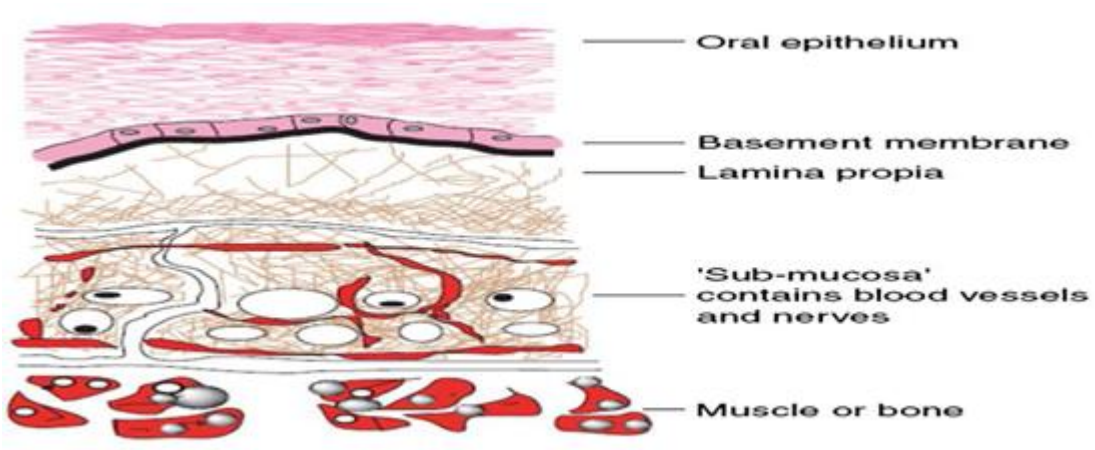

Fig.1: Schematic diagram of Buccal mucosa

ODTs involve the following mechanisms to achieve the desired fast dissolving characteristics.

1. Water must quickly enter the tablet matrix to cause rapid disintegration and instantaneous dissolution of the tablet.

2. Incorporation of an appropriate disintegrating agent or highly water-soluble excipients in the tablet formulation.

3. There are some mechanisms mentioned below by which the tablet is broken down into smaller particles and then subsequently results in a solution or suspension of the drug.

The mechanisms are-

- High swellability and disintegration
- Chemical reaction
- Capillary action

ADVANTAGES

- No need for water to swallow the tablet.
- Compatible with taste-masking agents and have a pleasing mouth feel.
- Can be easily administered to pediatric, elderly and mentally disabled patients.
- No residue in the oral cavity after administration.
- Manufacturing of the tablets can be done using conventional processing and packaging equipments at minimum cost.
- Allows high drug loading.
- Accurate doses can be given as compared to liquids.
- Dissolution and absorption of the drug is fast, offering a rapid onset of action.

- No risk of suffocation due to physical obstruction when swallowed, thus offering improved safety.

- It is reported that swallowing difficulty (dysphasia) due to diseases like motion sickness and allergic attacks may cause noncompliance and ineffective therapy. In these cases, comfort and quality of life will be enhanced via ODTs.

- ODTs are also suitable for sustained and controlled release actives.

- Unit packaging.

- Conventional manufacturing equipment.

- Cost effective.

- Good chemical stability compared to conventional oral solid dosage form.

- Product differentiation, product promotion, patent extension, and lifestyle management are all new business opportunities.

- Provides rapid drug delivery from dosage forms.

- Provides the advantage of liquid medication in the form of solid preparation.

- Rapid drug therapy intervention.

- No chewing needed.

- Adaptable and amenable to existing processing and packaging machinery.

- Rapid onset of action.

- ODTs have led to bioavailability enhancement which subsequently reduced dosing frequency and side effects.

- Safety profiles may be improved for drugs that produce significant amounts of toxic metabolites mediated by first-pass liver metabolism and gastric metabolism and for drugs that have a substantial fraction of absorption in the oral cavity and segments of the pregastric GIT.

LIMITATIONS

- The tablets commonly have insufficient mechanical strength. Hence, conscientious handling is necessary.

- The tablets may leave an unpalatable taste and grittiness in the oral cavity if not formulated properly.

- Drugs that have large doses can cause problems in formulating them into ODTs.

- Patients who simultaneously take anti-cholinergic drugs are not suitable candidates for ODTs.

- The administration of ODTs may not inherently result in a faster therapeutic onset, but it can circumvent problems such as difficulty in swallowing traditional solid oral dosage forms, particularly by pediatric and geriatric patients.

- The impetus behind developing an ODT includes clinical, medical, technical, business, and marketing advantages.

- The application of this technology is limited by the amount of drug that can be incorporated into each unit dose.

- For lyophilized dosage forms, the drug dose must be lower than 400 mg for insoluble drugs and less than 60 mg for soluble drugs because they dissolve quickly,

- ODTs cannot provide controlled or sustained release, except those that contain slow-dissolving, micro particulate-coated drugs, which quickly disperse and are swallowed.

- Hygroscopic characteristics and thermal and humidity sensitivity of ODTs can influence their physical integrity and lead to stability problems. Hence, using special materials is essential for their packaging.

- Decreased amount of saliva in patients on anticholinergic medicines may affect the bioavailability of ODTs.

- If significantly higher plasma levels and systemic exposure have been observed, then pregastric absorption leading to the avoidance of first-pass metabolism may play an important

role. This situation may have implications for drug safety and efficacy, which may need to be addressed and assessed in a marketing application for an ODT.

COMPONENTS USED IN THE FORMULATING OF ODTs

Drug candidate: When choosing a suitable drug candidate to produce orally disintegrating tablets, several variables should be addressed. The final features of a medicine for oral dissolution and pregastric absorption for fast-dissolving tablets are as follows:

1. Free from bitter taste

2. Low-dose drugs preferably less than 50 mg.

3. Small to moderate molecular weight

4. Good solubility in water and saliva

5. Partially unionized at oral cavity pH

6. Ability to diffuse and partition into the epithelium of upper GIT (log >1, or preferably>2)

7. Ability to permeate oral mucosal tissue.

8. Short half life and frequent dosing drugs are unsuitable for ODT.

9. Drug should have good stability in saliva and water.

ODT was developed by researchers for a variety of medications used in therapy that require a rapid peak plasma concentration to obtain the desired pharmacological response. Neuroleptics, cardiovascular agents, analgesics, antiallergics, anti-epileptics, anxiolytics, sedatives, hypnotics, diuretics, anti-parkinsonism agents, anti-bacterial agents, and erectile dysfunction medications are just a few examples.

The following qualities, on the other hand, may make it inappropriate for use as an orally disintegrating tablet:-

1. Short half-life and frequent dosing.

2. Very bitter or otherwise unacceptable taste because taste masking cannot be successfully achieved.

3. Require controlled or sustained release.

4. Combination with anticholinergics.

5. Patients suffering from Sjogren's syndrome and those with less saliva secretion and not suitable for ODT dosage form.

6. Drugs showing altered pharmacokinetic behavior like selegiline, apomorphine and buspirone are not suitable for ODT.

Brand name	Active ingredient	Company
Domray MD	Domperidone	Ray Remedies
Velrid MD	Domperidone	Shreyam Health Care
Vomidon MD	Domperidone	Olcare Lab
Zotacet MD	Cetirizine HCl	Zota Pharma
Olanex Instab	Olanzapine	Ranbaxy
Manza RDT	Olanzapine	Mano Pharma (Orchid)
Romilast	Montelukast	Ranbaxy
Torrox MT	Rofecoxib	Torrent
Ziflam	Rofecoxib	Kopram
Doloroff	Rofecoxib	Indoco
Rofaday MT	Rofecoxib	Lupin
Dolib MD	Rofecoxib	Panacea
Orthoref MD	Rofecoxib	Biochem
Rbcox-25 MD	Rofecoxib	Shalman Pharma
Roffec MD	Rofecoxib	Excare Lab
Roftab MD	Rofecoxib	Oicare Lab
Zofex-25 MD	Rofecoxib	Zota Pharma
Valus	Valdecoxib	Glenmark
Nency MD	Nimesulide	Zenon Health Care
Nexus MD	Nimesulide	Lexus
Nimex MD	Nimesulide	Mexon Health Care
Nimez-MD	Nimesulide	Zota Pharma
Insure-MD	Nimesulide	Suzen Pharma
Nimulid-MD	Nimesulide	Panacea
Olnim-MD	Nimesulide	Olcare Lab
Sulbid-MD	Nimesulide	Alpic Remedies
Topmide	Nimesulide	Antigen Health Care
Mosid MT	Mosapride	Torrent

Fig.2: Orally disintegrating tablet products available in Indian market

Excipients:

The fast dissolving property of ODTs necessitates rapid water absorption into the tablet matrix, which includes increasing the tablet's porosity structure, incorporating a suitable disintegrating agent, and using water-soluble excipients in the formulation. At least one super disintegrant, a diluent, a lubricant, a permeabilizing agent, sweeteners, and flavorings are included among the excipients used in ODTs.

Also swelling agents are optionally used as common excipients in ODT. The qualities of ideal bulk excipients for orally disintegrating dosage forms are as follows:

1. Disperses and dissolves in the mouth within a few seconds without leaving any residue.

2. Masks the drug’s offensive taste and offers a pleasant mouth feel.

3. Enables sufficient drug loading and remains relatively unaffected by changes in humidity or temperature.

The role of excipients is important in the formulation of fast-melting tablets. The temperature of the excipients should be preferably around 30–35 degrees Celsius for faster-melting properties.

Excipient Selection Criteria

In Immediate release dosage forms, excipients balance the characteristics of the active substance. To avoid interactions with the active substance, a thorough understanding of the chemistry of these excipients is required. Another difficulty that formulators must handle is determining the cost of these substances. Excipients play a crucial role in the formulation of fast-melting tablets.

Table 1: Approved Excipients used in ODT formulations

Ingredient type	Example	Role
Superdisintegrant	Crospovidone, croscarmellose sodium, sodium starch glycolate, sodium carboxymethyl cellulose, microcrystalline cellulose, spray-dried lactose, acrylic acid, alginic acid, sodium alginate, soy polysaccharides, Isphagula husk pregelatinized starch, modified corn starch, ion exchange resins, gas evolving disintegrants	(i) Burst disintegration facilitator
Bulking material	Sugar and sugar-based derivatives (dextrose, fructose, isomalt, lactitol, maltitol, maltose, mannitol, sorbitol, starch hydrolysate, polydextrose, and xylitol)	(i) Textural properties (disintegration time) improver
Emulsifier	Alkyl sulfates, propylene glycol, lecithin, sucrose esters, sodium dodecyl sulfate, sodium lauryl sulfate, polyoxyethylene sorbitan fatty acid esters (Tweens)	(i) Disintegration accelerator (ii) Bioavailability enhancer of immiscible substances
Sweetener	Sodium saccharin, sugar alcohols, natural sugars (sugar, dextrose, fructose), sugars derivatives, aspartame, vanilla, bubble gum, grapefruit	(i) Bitter taste mask (ii) Tablets' acceptability enhancer
Flavor	Peppermint flavor, clove oil, bay oil, anise oil, eucalyptus oil, thyme oil, oil of bitter almonds, vanilla, citrus oils, fruit essences	(i) Patient compliance and acceptability improver

CHALLENGES IN FORMULATION OF ODTs

Mechanical strength and disintegration time: If the mechanical strength is higher, the disintegration period will be longer, so good collaboration between these two factors is always required.

Taste masking: Efficient taste masking of the bitter drugs must be done so that the taste of the drug is not felt in the oral cavity.

Mouth feel: The particles created after the ODT disintegration should be very tiny. After oral administration, ODT should not leave any residue in the mouth. The tongue sensation is improved by the addition of flavours and cooling substances such as menthol.

Sensitivity to environmental conditions: ODTs should have low sensitivity to environmental conditions such as humidity and temperature.

Cost: An affordable cost should be quoted for an ODT based on the technology used.

APPROACHES FOR PREPARATION OF ODTs

Various preparation processes based on different concepts have been established, resulting in varying qualities of ODTs in terms of mechanical strength, stability, mouth feel, taste, swallowability, dissolving profile, and bioavailability. Some of these innovations are protected by patents. The following are the basic pharmaceutical techniques for producing ODTs: The technology employed to make ODTs has an impact on their performance.

Spray drying

Pharmaceutical and biochemical procedures make extensive use of spray drying techniques. Spray drying is a quick and cost-effective approach to get rid of solvents while also producing highly porous and fine powders. Hydrolyzed and non-hydrolyzed gelatins are used as supporting agents, mannitol is used as a bulking agent, and croscarmellose sodium or sodium starch glycolate is used as a disintegrating agent. To promote disintegration and dissolving behavior, an acidic material (e.g., citric acid) or an alkali material (e.g., sodium bicarbonate) is utilized. When tablets made from spray-dried powder were put in an aqueous media, they revealed a disintegration time of 20 seconds.

Sublimation

Due to the reduced porosity of the tablets, which restricts water penetration into the matrix, compressed tablets containing highly water-soluble components can have a sluggish dissolving rate. Volatile compounds are compacted into tablets using traditional methods, and these volatile materials can be eliminated via sublimation, resulting in very porous structures. Ammonium carbonate, urea, ammonium bicarbonate, camphor, and hexa methylene tetramine are some of the volatile materials that can be employed. Thymol, menthol, camphor, an organic acid like adipic acid, and fatty acids like arachidic acid, myristic acid, capric acid, and palmitic acid were utilized as volatile materials in a few cases, with sublimation temperatures ranging from 40 to 60 degrees Celsius. In the oral cavity, the disintegration time was found to be around 25 seconds.

Freeze drying

A frozen drug solution or a suspension containing structure-forming excipients undergoes lyophilization, which entails the elimination of solvents. The tablets produced by this method are typically very light and have porous features that allow for rapid dissolving or disintegration. Lyophilization is performed at a very low temperature to avoid thermal effects that could affect drug stability during processing. During the shelf life of the freeze-dried dosage form, there are few worries about stability. Excipients and pharmacological ingredient may develop a glassy amorphous structure because of the drying process.

Molding

Water-soluble components are used to make molded tablets. A solvent is sprayed on the powder combination (usually water or ethanol). Under pressure, the mixture is shaped into tablets. The pressure utilized should be less than that used in traditional tablet compression. Compression molding is another name for this procedure. The solvent can be removed by air drying. Because of the decreased pressure, a very porous structure is formed, which aids in dissolving. To boost the dissolving rate, the powder mixture should be run through a very fine screen. Because of their extremely water-soluble sugar components, molded tablets disintegrate faster and have a better taste. Molded tablets, on the other hand, are not known for their mechanical robustness. The risks of the molded tablets breaking during tablet handling and blister pocket opening are extremely high. The disintegration rate is reduced when hardness-increasing compounds are employed in the formulation. Using non-conventional equipment and multistep methods can increase the mechanical strength and breakdown of the tablets.

Mass extrusion

The active blend is softened using a solvent mixture of water-soluble polyethylene glycol and methanol in a bulk extrusion technique. Extrusion of softened substance using a syringe or extruder produces a cylinder of the product, which is subsequently cut into even segments with a hot blade to form tablets. Through this technique, we can mask the bitter taste of the drug by coating granules using compounds like Eudragit E 100, Ethylcellulose, Hydroxy Propyl Methyl Cellulose (HPMC), Hydroxy Propyl Cellulose (HPC), Polyvinyl alcohol, and Polyvinyl acetate.

Direct compression

Direct compression is the most straightforward and cost-effective method of tablet production. This approach can be used to make ODT by selecting optimal excipient combinations that enable quick disintegration and high physical resistance. Because of its aqueous solubility, sweetness, appealing mouth feel, and effective taste masking, sugar-based excipients are commonly utilized as bulking agents. The traditional compression process produces less friable tablets that degrade more slowly. The compression method, which can be used with or without wet granulation, is a quick and inexpensive way to make tablets with appropriate structural strength.

PATENTED TECHNOLOGIES

Zydis technology

R.P.Scherer, Inc Zydis.'s technology was the first to be commercialized for the production of new generation tablets. The first marketed new technology tablet was Zydis, the most well-known of the fast-dissolving/disintegrating tablet preparations. After being placed on the tongue for a few seconds, the tablet dissolves in the mouth. Zydis is a freeze-dried tablet in which the medication is physically entrapped or dissolved in a matrix made up of two components: a saccharide, such as mannitol, and a polymer. When Zydis units are kept in the mouth, the freeze-dried structure instantly disintegrates and does not need to be swallowed with water. To provide strength during handling, polymers such as gelatin, and dextran are used. Mannitol or sorbitols are utilised to achieve crystallinity, attractiveness, and durability. Preservatives (e.g., parabens) are used to prevent microbiological development; permeation enhancers (e.g., sodium lauryl sulphate) are used to promote transmucosal permeability; pH adjusters (e.g., citric acid) are used to maximise chemical stability; flavours and sweeteners are used to improve patient compliance to accomplish quick disintegration, Water is utilised in the manufacturing process to ensure the manufacture of porous units. Gums prevent scattered particles from settling throughout the production process. Collapse inhibitors, such as gelatin, prevent Zydis units from shrinking during the freeze-drying process or long-term storage. Because the product is light and fragile, it must be distributed in a particular blister pack.

Orasolv technology

Cima's first fast-dissolving disintegrating dose form was OraSolv. This method masks the taste of the active medication and includes a dissolving agent. The action of an effervescent substance activated by saliva causes ODT to disintegrate in the mouth. The amount of effervescent agent in a tablet is typically 20-25 percent of the overall weight. An acid source (citric, tartaric, malic, fumaric, adipic, and succinic acids) and a carbonate source make up the most common effervescent disintegration pair (sodium bicarbonate, sodium carbonate, potassium bicarbonate and potassium carbonate, magnesium carbonate).To maintain the coating's integrity, the microspheres are loosely squeezed. The mechanical strength of the OraSolv formulations is one of its key drawbacks. As a result, Cima designed a unique OraSolv handling and packaging method. Manufacturing necessitates a regulated atmosphere with low relative humidity and the use of moisture-resistant blisters to protect the final tablets.

Durasolv technology

Durasolv is CIMA's second-generation fast-dissolving or disintegrating tablet formulation, designed to provide stronger tablets for use in blisters or bottles. Because of the higher compaction pressure used during tableting, Durasolv has a substantially higher mechanical strength. Durasolv has one drawback: the technology is incompatible with bigger quantities of active chemicals because the formulation is compressed under high pressure. Durasolv's drug powder covering may crack during compaction, exposing bitter-tasting pharmaceuticals to the patient's taste receptors. As a result, this method is suitable for tablets containing a small number of active components.

Wow tab technology

The WOW in WOWTAB denotes that the tablet should be taken without water. Sugar and sugar-like excipients are used in this technology. The two types of saccharides are mixed to create a tablet formulation with sufficient hardness and rapid dissolving. Maltose, mannitol, sorbitol, and oligosaccharides are examples of high moldability saccharides, while lactose, glucose, mannitol, and xylitol are examples of low moldability saccharides (rapid dissolution). The tablets made with this method will be hard enough to maintain the physical features of the dosage form during manufacture until they come into touch with moisture in the mouth, such as saliva. The WOWTAB formulation is more environmentally stable than

Zydis and Orasolv due to its substantial hardness.

Cotton candy technology

This method gets its name from the fact that it uses an incomparable spinning motor to create a floss-like crystalline structure that looks like cotton candy. The candy floss procedure is also known as the cotton candy process. Candy floss or a shear form matrix is used to create a mouth-dissolving tablet. It entails the simultaneous process of flash melting and spinning to generate a matrix of polysaccharides or saccharides. To increase flow characteristics and compressibility, the matrix is partially recrystallized. After that, the candy floss matrix is milled and mixed with active chemicals and excipients before being compressed into ODT. This method can handle bigger medication doses and has better mechanical strength. However, the usage of this technique is limited due to the high process temperature.

Oraquick technology

A proprietary flavor masking technology is used in the Oraquick fast-dissolving/ disintegrating tablets formulation. Because there are no solvents used in this taste masking procedure, it is faster and more efficient. Because low-heat is produced during processing, this approach is excellent for heat-sensitive pharmaceuticals. The matrix that surrounds and protects the medication powder in microencapsulated particles, according to KV Pharmaceuticals, is also more flexible. This method produces tablets with a pleasant flavor masking and rapid dissolving in a matter of seconds.

Nanocrystal technology

Pharmacokinetic benefits of orally delivered nanoparticles (2 microns) in the form of a fast disintegrating tablet matrix are provided by Nano Crystal Fast Dissolving technology. The drug substance's nanocrystal colloidal dispersions are blended with water-soluble GRAS (Generally Regarded As Safe) components, then placed into blisters and lyophilized. This procedure avoids granulation, mixing, and tableting, which has greater advantages for highly potent and hazardous medications. Elans' proprietary Nanocrystal technology can help with formulation and increase drug activity and final product qualities for fast-dissolving tablets. The surface area of a particle increases as its size decreases, resulting in a faster dissolving rate.

Shear form technology

A 'Floss' shearform matrix is prepared in this method. Flash heat processing is used on feedstock that has been prepared using a sugar carrier. Sugar is subjected to centrifugal force and a temperature gradient in this process, which causes the mass's temperature to rise and so creates an internal flow condition, allowing a portion of it to move about the mass. The floss then exits through the spinning head, which flings it under centrifugal force and pulls it into long and thin floss threads, which are usually amorphous. The floss is then cut and recrystallized to provide a uniform flow and make blending easier .The recrystallized matrix, active medication, and other excipients are then combined together, and the tablets are ultimately crushed. Before recrystallizing the floss, the active medication and additional excipients can be mixed in. Due to the quick solubilization of sugars in the presence of saliva, the tablets produced by this technique are highly porous in nature and have a very pleasant tongue feel.

Pharma burst technology

SPI Pharma has a patent on the Pharmaburst technology. Pharmaburst technology employs off-the-shelf coprocessed excipients to create an ODT that dissolves in 30- 40 seconds, depending on the type of active ingredients and loading. The amount of pharmaburst needed in a formulation is determined by the tablet's active components. A dry mixture containing medicine, flavor, and lubrication is compacted into a tablet on a typical tablet press using standard machinery. Under typical temperature and humidity conditions, the manufacturing process can be completed. Blister packs or bottles can be used to package the tablets.

Frosta technology

This technology is patented by Akina. Frosta technology is based on compressing highly plastic granules at low pressure to generate robust, high-porosity tablets. Three types of components make up the extremely plastic granules: a porous and plastic substance, a water penetration enhancer, and a binder. The porous plastic material is mixed with a water penetration enhancer before being granulated with a binder. Almost any medicine, including aspirin, loratidine, caffeine, and folic acid, as well as vitamins and dietary supplements, can be tested using this technology. The highly plastic granule technique results in fast-melting pharmaceutical tablets with good hardness and disintegration times ranging from a few seconds to 30 seconds, depending on tablet size.

EVALUATION OF ODTs

Some unique tests, as well as the evaluation characteristics of tablets stated in the Pharmacopoeias, must be performed to evaluate ODTs. The quality of physicochemical qualities of blends determines the quality of a tablet once it has been formulated. Mixing involves several formulation and process variables, all of which can alter the characteristics of the mixes generated.

A. Evaluation of blends before compression:

These are the Precompression parameters.

The various characteristics of blends to be tested before compression are:

The angle of repose: The funnel method is used to determine the angle of repose. A funnel is used to collect the precisely weighed blend. The funnel's height is adjusted so that the funnel's tip just brushes against the apex of the blend heap. The drug-excipient mixture is allowed to run freely through the funnel and onto the surface. The powder cone's diameter is measured, and the angle of repose is determined using the equation below.

$$\tan \Theta = h/r$$

where,

h and r are the height of cone and the radius of cone base respectively.

An angle of Repose less than 30° shows the free flowing of the material.

The angle of repose demonstrates frictional force in a loose powder. When the angle is lower than 30 for a given powder, it represents free-flowing behavior.

Bulk density:

Pouring a weighed quantity of mix into a graduated cylinder and measuring the volume and weight yields the apparent bulk density. The following formula can be used to compute bulk density:

Bulk density = Weight of the powder / Volume of the packing.

Bulk density is directly related to particle size and the adhesion tendency; hence, it is helpful for the selection of packing materials and transportation considerations.

Tapped density:

A graduated cylinder carrying a known mass of drug-excipients blend is used to determine it. At 2-second intervals, the cylinder is permitted to fall from a height of 10 cm onto a hard surface under its own weight. The tapping is kept going until there is no more change in volume. The following formula can be used to compute tapped density:

Tapped Density = (Weight of the powder/volume of the tapped packing)

Compressibility index:

The Compressibility Index of the blends is determined by compressibility index. Compressibility Index can be calculated by using the following formula:

Compressibility Index (%) = [(TD-BD) X 100] / TD]

Hausner's ratio:

A similar index to indicate the flow properties can be defined by Hausner's ratio. Hausner's ratio can be calculated by using the following formula:

Hausner's ratio = (Tapped density x 100)/ (Poured density)

When the Hausner ratio is lower than 1.25, flowability is good, while excellent compressibility is seen for Carr's index less than 15.

Void Volume:

The volume of the spaces is known as the void volume "V" and is given by the formula:

$$V = V_b - Vp$$

Where,

Vb = Bulk volume (volume before tapping)

Vp = True volume (volume after tapping)

Porosity:

The porosity € of powder is defined as the ratio of void volume to the bulk volume of the packaging. The porosity of the powder is given by the following formula:

$$€= Vb – Vp / Vp =1- Vp/Vb$$

Porosity is frequently expressed in percentage and is given as:

$$\% € = (1 – Vp / Vb) X 100$$

The porosity of powder indicates the type of packaging when subjected to vibrations, when stored, or in tablet machine when passed through hopper or feed frame.

B. Evaluation of Tablets:

These are the Post compression parameters.

All the formulated ODTs were subjected to the following quality control tests.

Weight variation:

The weight variation test is carried out to ensure uniformity in the weight of tablets in a batch. First the total weight of 20 tablets from each formulation is determined and the average is calculated. The individual weight of each tablet is also determined to find out the weight variation.

Hardness:

The hardness of tablet is an indication of its strength. Measuring the force required to break the tablet is considered. The force is measured in Kg and the hardness of about 5-6 Kg/cm2 is satisfactory for uncoated tablets. Hardness of 10 tablets from each formulation is determined by Monsanto hardness tester, Pfizer hardness tester etc.

Friability test:

Friability is the loss of weight of tablet in the container due to removal of fine particles from the surface. Friability test is carried out to access the ability of the tablet to withstand abrasion in packaging, handling, and transport. Roche friabilator is employed for finding the

friability of the tablets. Weigh the 20 tablets from each batch and place in Roche friabilator that will rotate at 25 rpm for 4 minutes. Dedust the tablets and weigh again. The percentage of friability can be calculated using the formula:

% Friability = [(W1-W2)100]/W1

Where,

W1= Weight of tablet before test,

W2 = Weight of tablet after test

Disintegration test:

The USP disintegration apparatus contains six glass tubes that are “3 long, open at the top, and held against 10” screen at the bottom end of the basket rack assembly. One tablet is placed in each tube and the basket rack is placed in 1 liter beaker of distilled water at 37± 2°C, such that the tablets remain below the surface of the liquid on their upward movement and descend not closer than 2.5cm from the bottom of the beaker.

Mechanical strength:

Tablets should possess adequate mechanical strength to bear shocks of handling in manufacturing, packaging, and shipping. Crushing strength and friability are two important parameters for the determination of mechanical strength. Crushing Strength or Tablet Tensile strength is the force required to break a tablet by compression in the radial direction, it is important to note that excessive crushing strength significantly reduces the disintegration time. The crushing strength of the tablet is measured by using Pfizer hardness testers. Tensile strength for crushing (T) is calculated using equation:

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

Where,

F is the crushing load, and d and t denote the diameter and thickness of the tablet respectively.

Uniformity of dispersion:

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

Wetting time:

The wetting time of the tablets is measured using a simple procedure. Place the five circular tissue papers of 10 cm diameter in a Petri dish containing 0.2% w/v solution (3ml). A tablet is carefully placed on the surface of the tissue paper. The time required for developing blue color on the upper surface of the tablet is noted as the wetting time.

Water absorption ratio:

A small piece of tissue paper folded twice is placed in a small Petri dish 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. The water absorption ratio, R is determined by using following formula:

$$R = 100 \times Wa-Wb / Wb$$

Where,

Wb is the weight of tablet before water absorption

Wa is the weight of the tablet after water absorption

Taste/ Mouth sensation:

Mouth-feel is critical, and patients should receive a product that gives a pleasant feel. One tablet from each batch is tested for the sensation by placing the tablet on the tongue. The healthy human volunteers are used for the evaluation of mouth feel. Taste evaluation is done by a panel of 5 members using the time-intensity method. Sample equivalent to 40 mg i.e. dose of drug is put in the mouth for 10 seconds and record taste instantly and then after 10 seconds, 1, 2, 4 and 6 minutes. Volunteers' opinion for the taste is rated by giving different score values i.e.

0 = good,

1 = tasteless,

2 = slightly bitter,

3 = bitter,

4 = awful

In-vitro disintegration test:

In-vitro disintegration time is measured by dropping a tablet in a beaker containing 50 ml of Sorenson's buffer pH 6.4. Three tablets from each formulation are randomly selected and in vitro dispersion time is carried out.

In-Vivo disintegration test:

The test is carried out on 2 or 3 tablets in the mouth and the time in second taken for complete disintegration of the tablet is measured.

In vivo, the determination of disintegration time may be carried out with randomly chosen healthy volunteers. First, volunteers are asked to wash their mouths. A tablet is put on their tongue, and the time taken for the disintegration of the last granule will be measured. If the tablets contain active substances with side effects on healthy volunteers, prior permission must be acquired from the Board of Ethics.

In-Vitro dissolution test:

In-vitro dissolution study is performed by using USP Type II Apparatus (Paddle type) at 50 rpm. Phosphate buffer pH 6.4, 900 ml is used as dissolution medium which maintained at 37±0.5°C. Withdraw aliquot of dissolution medium (10 ml) at specific time intervals (2 min) and filter. The amount of drug dissolved is determined by suitable analytical techniques.

PACKAGING CONSIDERATIONS

Packing is one of the essential steps in ODT development. As excipients used in the formulation of ODTs should disintegrate/dissolve in a minimum amount of water, and, they may attract moisture from the surrounding; therefore, special consideration is needed for their storage like a dry place. In addition, ODTs prepared by diverse techniques have different mechanical strengths; therefore, they need distinct packing.

For example, ODTs designed by Zydis are porous and have less physical resistance and sensitivity to moisture.

CONCLUSION

Orally disintegrating tablets (ODTs) have better patient acceptance and compliance and may offer improved biopharmaceutical properties, improved efficacy, and better safety compared with conventional oral dosage forms. The future potential for ODTs is promising because of the availability of new technologies combined with strong market acceptance and patient demand. Dozens of ODT products have been commercialized, and the market size for ODTs will continue to expand as the technology is used to deliver large-molecular weight biopharmaceutical therapeutics such as proteins and peptides when coupled with the appropriate permeation enhancers. By paying close attention to advances in technologies, pharmaceutical companies can take advantage of ODTs for product line extensions or first-to-market products.

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