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Review Article

ORAL DISPERSIBLE TABLETS: AN OVERVIEW; DEVELOPMENT, TECHNOLOGIES AND EVALUATION

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ABSTRACT

Now-a-days, orodispersible drug delivery systems are extensively used to improve bioavailability and patient compliance. Over the past three decades, orodispersible tablets (ODTs) have gained considerable attention as a preferred alternative to conventional tablets and capsules due to better patient compliance, improved solubility and stability profiles. The purpose of the article is to review potential advancements of ODT technology in drug delivery applications. Various techniques employed to prepare ODTs include direct compression method, freeze drying, spray drying, tablet moulding, sublimation and mass extrusion. ODTs could be preferred choice especially with those drugs sensitive to GI and for patients under category of pediatrics, geriatrics, bedridden, postoperative and who may have difficulty in swallowing the conventional tablets and capsules.ODTs are solid dosage forms containing medicinal substances which disintegrate rapidly, usually in a matter of seconds, when placed on the tongue.ODTs render enhanced acceptability due to its patient compliance as well as improved bioavailability and stability. This article reviews recent trends undertaken to develop ODTs, new ODTs technologies, suitability of drug candidate and characterization of ODTs.

Keywords: Orodispersible tablets (ODTs), Improved bioavailability and super disintegrates..

INTRODUCTION

For most therapeutic agents used to produce systemic effects, the oral route still represents the preferred way of administration owing to its several advantages and high patient compliance compared to many other routes [1].

Orodispersible tablets are also called as orally disintegrating tablets, mouth-dissolving tablets, rapid dissolving tablets, fast-disintegrating tablets, fast-dissolving tablets. Recently, European Pharmacopoeia has used the term orodispersible tablets. This may be defined as uncoated tablets intended to be placed in the mouth where they disperse readily within 3 min before swallowing [4].

Despite of tremendous advancements in drug delivery, the oral route remains the perfect route for the administration of therapeutic agents because of low cost of therapy, ease of

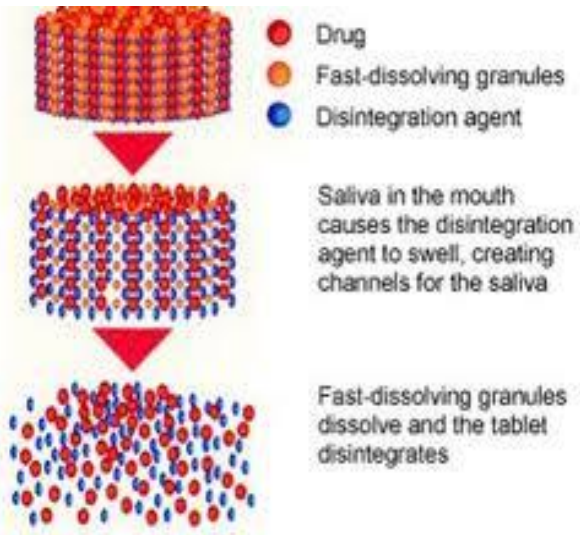

Fig.1: Fast dissolving tablets

administration, accurate dosage, self-medication, pain avoidance, versatility, leading to high levels of patient compliance. Tablets and capsules are the most popular dosage forms. But one important drawback of such dosage forms is 'Dysphasia' or difficulty in swallowing. This is seen to afflict nearly 35% of the general population. This disorder is also associated with a number of conditions like:

1. Parkinsonism
2. Motion sickness
3. Unconsciousness
4. Elderly patients
5. Children
6. Mentally disabled persons
7. Unavailability of water [5]

The oral route remains the perfect route for the administration of therapeutic agents because the low cost of therapy, manufacturing and ease of administration lead to high levels of patient compliance. Many patients have difficulty swallowing tablets and hard gelatin capsules and consequently do not take medications as prescribed. It is estimated that 50% of the population is affected by this problem, which results in a high incidence of noncompliance and ineffective therapy. The demand for solid dosage forms that can be dissolved and suspended in water, chewed, or rapidly dissolved in the mouth is particularly strong in the pediatric and geriatricmarkets, with further application to other patients who prefer the convenience of a readily administered dosage form[7].

The oral route of administration is considered as the most widely accepted route because of its convenience of self administration, compactness and easy manufacturing[2][3].

When put in the mouth, these dosage forms disintegrate instantly to release the drug, which dissolves or disperses in the saliva. Thereafter, the drug may get absorbed from the pharynx and oesophagus or from other sections of g.i.t as the saliva travels down. In such cases, bioavailability is significantly greater than that observed from conventional tablet dosage form[6].

Fast dissolving tablets are gaining prominence as new drug delivery systems. These dosage forms dissolve or disintegrate in the oral cavity within a matter of seconds without the need of water or chewing. These are useful for pediatric, geriatric and also dysphagia patients, leading to improved patient compliance. Nonetheless, oral dosing remains the preferred mode of administration for many types of medication due to its simplicity, versatility, convenience, and patient acceptability. In recent years, fast dissolving drug formulations have been developed to overcome problems related to swallowing difficulties. When such tablets are placed in the oral cavity, saliva quickly penetrates into the pores to cause rapid tablet disintegration[8].

IDEAL PROPERTIES OF ODTS:

ODTs are being preferred as advanced dosage form in most instances over conventional immediate release dosage form for various categories of drugs. It is expected to bear certain remarkable features that make the mideal. For instance ODT disintegrate or dissolves in mouth within a very short time. Further, they do not require water on administration, present acceptable taste masking properties, should have high drug loading capacity, pleasing mouth feel, stable in environmental condition and must not leave any residue in mouth after oral administration[9].

Due to their rapid presentation of drug at the buccal cavity ODTs would be always dosage form of choice in case of drugs that are unsuitable to be delivered through GI for many reasons. The advantages offered by ODTs over immediate release formulations may include ease of formulation designing and manufacturing, unit packaging, easy to handle by patients[3][6][10], no need of water to administer, rapid disintegration of tablet results in quick dissolution and rapid absorption which provide rapid onset of action that may lead to enhanced therapeutic efficiency due to increased bioavailability[11].

LIMITATIONS OF ODTS: [12]

Most of times soluble diluents used for formulating ODTs might render hygroscopic dosage which may lead to stability issues.

The tablets may leave unpleasant taste and/or grittiness in mouth if not formulated properly.

Specialized packing might be required for hygroscopic and light sensitive drugs.

Precautions to be taken while administering immediately after removing from pack.

Light sensitive drugs, ODTs may not be suitable as no option for film coating.

Salient features of ODT: [13]

The risk of chocking or suffocation during oral administration of conventional formulation due to physical obstruction is avoided, thus providing improved safety.

Rapid drug therapy intervention.

After oral administration they should leave minimal or no residue in mouth.

It should be dissolve or disintegrate in mouth within few seconds.

High drug loading should be allowed.

They should be compatible with taste masking and other excipients.

They should be less sensitive to environmental conditions such as humidity and temperature.

The mouth feel should be pleasant.

They must have sufficient strength to withstand the rigors of the manufacturing process and during the post manufacturing handling[14].

Advantages of ODT: [15]

Ease of administration to patients who refuse to swallow a tablet, such as pediatric, geriatric, mentally ill, disabled and uncooperative patients.

Rapid dissolution of drug and absorption may produce rapid onset of action.

Pregastric absorption can result in improved bioavailability, and as a result of reduced dosage, improved clinical performance by reducing side effects.

No need of water to swallow the dosage form, which is highly convenient feature for patients who are travelling and do not have immediate access to water.

Convenience of administration and accurate dose as compared to liquids.

Some drugs are absorbed from the mouth, pharynx and oesophagus as the saliva passes down into the stomach; in such cases bioavailability of drugs is increases.

Good mouth feel property of ODTs helps to change the psychology of medication as "bitter pill" particularly in pediatrics' patients.

Ability to provide advantages of liquid medication in the form of solid preparation.

New business opportunities: product differentiation, line extension and lifecycle management, exclusivity of the product promotion and patent-life extension[16].

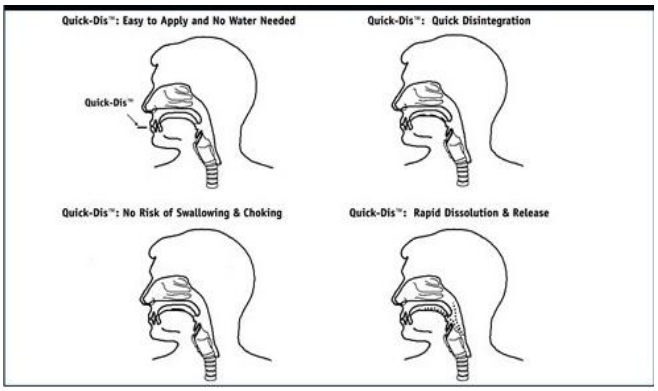

Fig.2: Advantage of ODT

Disadvantages of ODT: [17]

Rapid disintegrating tablets are hygroscopic in nature so must be kept at controlled environment i.e. humidity and temperature.

For properly stabilization and safety of stable product, ODT requires special packaging.

Usually have insufficient mechanical strength. Hence, careful handling is required.

Leave unpleasant taste and/or grittiness in mouth if not formulated properly [18].

TECHNIQUES FOR PREPARING ORODISPERSIBLETABLETS:

Freeze Drying/ Lyophilization:A process in which water is sublimated from the product after freezing is called freeze drying. Freeze dried forms offer more rapid dissolution than other available solid products. The lyophilization process imparts glossy amorphous structure to the bulking agent and sometimes to the drug, thereby enhancing the dissolution characteristics of the formulation. However, the use of freeze drying is limited due to high cost of the equipment and processing. Other major disadvantages of the final dosage forms include lack of physical resistance in standard blister packs. R. P. Scherer patented Zydis technology by employing freeze drying process for the preparation of mouth dissolving tablets on the basis of patents issued to Gregory et al. Jaccard and Leyder also utilized lypholization to prepare orodispersible tablets of various drugs[19][20].

Moulding:Tablets produced by moulding are solid dispersions. Physical form of the drug in the tablets depends whether and to what extent it dissolves in the molten carrier. The drug can exist as discrete particles or micro particles dispersed in the matrix. It can dissolve totally in the molten

carrier to form solid solution or dissolve partially in the molten carrier and the remaining particles stay undissolved and dispersed in the matrix.

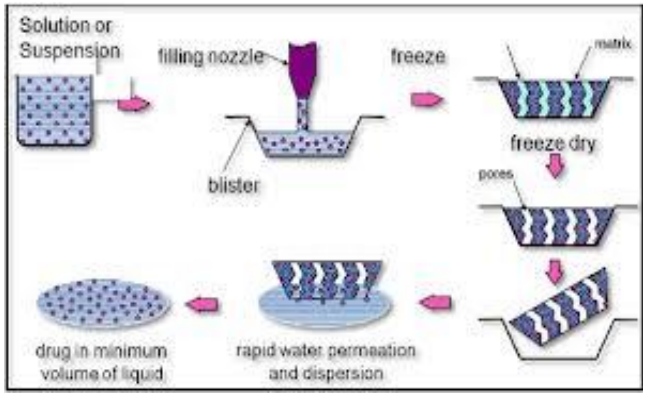

Fig.3: Vacuum evaporation without lyophilization

Disintegration time, drug dissolution rate and mouth feel will depend on the type of dispersion or dissolution. Moulded tablets disintegrate more rapidly and offer improved taste because the dispersion matrix is, in general made from water soluble sugars. Moulded tablets typically do not possess great mechanical strength. Erosion and breakage of the moulded tablet often occur during handling and opening of blister packs[21][22].

Sublimation:Because of low porosity, compressed tablets composed of highly water-soluble excipients as tablet matrix material often do not dissolve rapidly in the water. Porous tablets that exhibit good mechanical strength and dissolve quickly have been developed.

Inert solid ingredients (ex. urea, urethane, ammonium carbonate, camphor, naphthalene) were added to other tablet excipients and the blend was compressed into tablet. Removal of volatile material by sublimation[23].

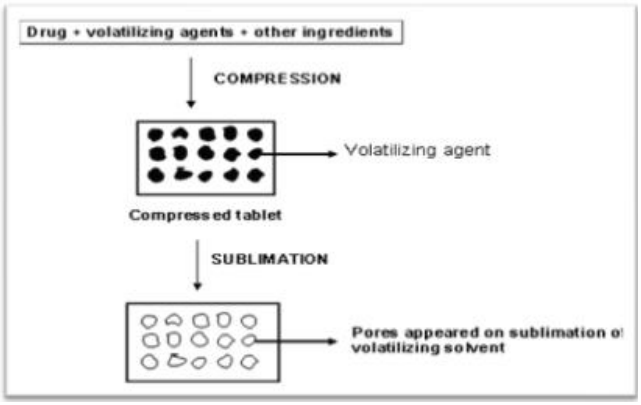

Fig.4: Sublimation

Sublimation generated a porous structure. Compressed tablets containing mannitol and camphor have been prepared by sublimation technique. The tablets dissolve within 10-20 seconds and exhibit sufficient mechanical strength for practical use[24].

Spray Drying:Spray drying can be used to prepare rapidly dissolving tablets. This technique is based upon a particulate support matrix that is prepared by spray drying an aqueous composition containing support matrix and other components to form a highly porous and fine powder. This is then mixed with active ingredient and compressed into tablet. Allen and Wang have employed spray drying technique, to prepare orodispersible tablets[25][26].

Mass Extrusion:This technology involves softening the active blend using the solvent mixture of water soluble polyethylene glycol, using methanol and expulsion of softened mass through the extruder or syringe to get a cylinder of the product into even segments using heated blade to form tablets. The dried cylinder can also be used to coat granules of bitter tasting drugs and thereby making their bitter taste[27][28].

Direct compression (dc):DC is the simplest and most cost effective tablet manufacturing technique for MDTs as they can be fabricated using conventional tablet manufacturing and packaging machinery and also due to availability of tabulating excipients with improved flow, compressibility and disintegration properties, especially tablet disintegrates, effervescent agents and sugar based excipients. Another DC based technology; Flash tab contains coated crystals of drug and micro granules along with Disintegrates [29]. In this technology, two types of Disintegrates are used: a disintegrating agent (e.g., modified cellulose), which has a high swelling force and a swelling agent (e.g., starch) which has a low swelling force [30].

Mizumoto et al., [31] have classified sugar-based excipients into two types based on their Mouldability and dissolution rate,

Type I saccharides (e.g., lactose and mannitol) exhibit low mouldability but high dissolution rate.

Typell saccharides (e.g., maltose and maltitol) exhibit high mouldability but low dissolution rate.

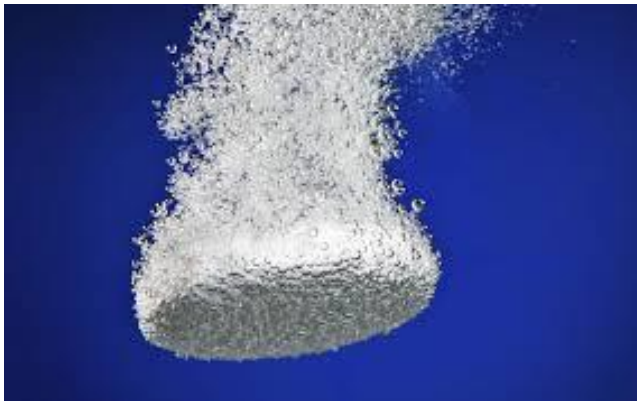

Fig.5 : Effervescent tablets

Cotton candy process:The FLASHDOSE® is a MDDDS manufactured using Shear form™ technology in association with Ceform TI™ technology to eliminate the bitter taste of the medicament [32][33].The Shear form technology is employed in the preparation of a matrix known as „floss", made from a combination of excipients, either alone or with drugs. The floss is a fibrous material similar to cotton-candy fibers, commonly made of saccharides such as sucrose, dextrose, lactose and fructose at temperatures ranging between 180–266 °F [34].The manufacturing process can be divided into four steps as detailed below.

- Floss Blend
- Floss Processing
- Floss Chopping and Conditioning
- Blending and Compression

Nanonization:A recently developed Nanomelt technology involves reduction in the particle size ofdrug to nanosize by milling the drug using a proprietary wet-milling technique . The nano crystals of the drug are stabilized against agglomeration by surface adsorption on selected stabilizers, which are then incorporated into MDTs. This technique is especially advantageous for poorly water soluble drugs[35].

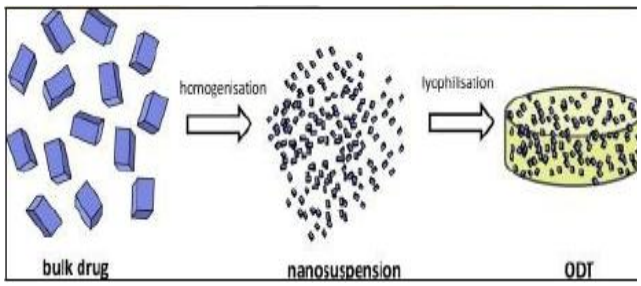

Fig.6: Nanonization

Phase transition process:It is concluded that a combination of low and high melting point sugar alcohols, as well as a phase transition in the manufacturing process, are important for making MDTs without any special apparatus. MDT was produced by Compressing powder containing erythritol (melting point:122°C) and xylitol (melting point: 93°, 95°C), and then heating at about 93°C for 15 min. after heating, the median pore size of the tablets was increased and tablet hardness was also Increased.The increase of the tablet hardness with heating and storage did not depend on the crystal state of the lower melting Point sugar alcohol [36].

Fast dissolving films:It is a new frontier in MDDDS that provides a very convenient means of taking medications and supplements. In this technique, a non-aqueous solution is prepared containing water soluble film forming polymer (pullulan, carboxyl methylcellulose, hydroxylpropyl methylcellulose, hydroxyl ethyl cellulose, hydroxyl propylcellulose, polyvinyl pyrrolidone, polyvinyl alcohol or sodium alginate, etc.), drug and other taste masking ingredients, which is allowed to form a film after evaporation of solvent. In case of a bitter drug, resin adsorbate or coated micro particles of the drug can be incorporated into the film [37].

Fig.7: Fast dissolving film

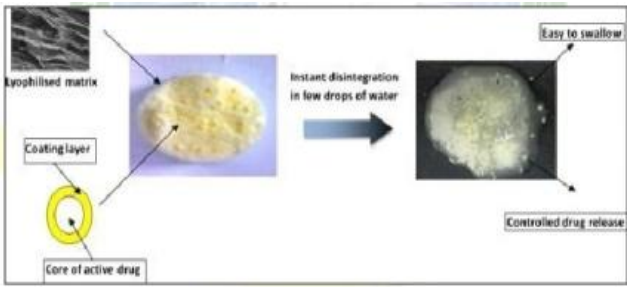

Fig.8: Mouth dissolving tablets

Mechanism of Action of Disintegrates:

The super disintegrates in the ODTs will act by different mechanisms. They are

- 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
- 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 /excipients and on tableting conditions [38].
- 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 [40][41].
- Because of Heat of Wetting (Air Expansion): When disintegrates 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 disintegrates and cannot describe the action of most modern disintegrating agents [40].
- 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 Disintegrantsare highlysensitive to small changes in humidity level and temperature, strict control of environment isrequired during manufacturing of the tablets [39].
- By Enzymatic Reaction: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 [40].

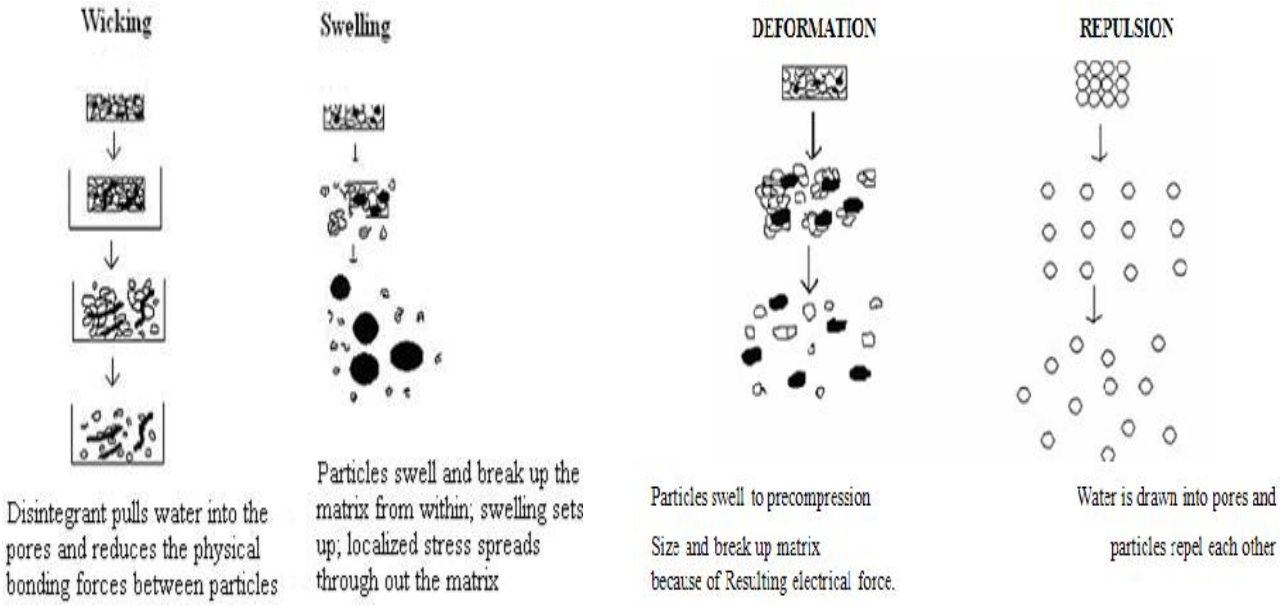

Fig.9: Swelling

Fig.10: Disintegration by enzymatic reaction

- Due to Disintegrating Particle/Particle Repulsive Forces:Another mechanism of disintegration attempts to explain the swelling of tablet made with "non-swellable" Disintegrates. Guyot- Hermann has proposed a particle repulsion theory based on the observation that nonswelling 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 [42].
- Due to Deformation: Hess had proved that during tablet compression, disintegrated particles get deformed and these deformed particles get into their normal structure when they come in contact with aqueous media or water. Occasionally, the swelling capacity of starch was improved when granules were extensively deformed during compression [43].

Super Disintegrates Used in MDTs:

As day's passes, demand for faster disintegrating formulation is increased. So, pharmacist needs to formulate Disintegrates i.e. Superdisintegrants which are effective at low concentration and have greater disintegrating efficiency and they are more effective intragranularly. This Superdisintegrants act by swelling and 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 [44].

Types of Super Disintegrates Used

Cross povidone

Microcrystalline cellulose

Sodium starch glycollate

Sodium carboxy methyl cellulose or cross carmelose sodium

Pregelatinzed starch

Calcium carboxy methyl cellulose

Modified corn starch. Sodium starch glycollate has good flow ability than crossCaramellose sodium.

Factors considered for selection of super disintegrantes:

It should produce mouth dissolving when tablet meets saliva in the mouth

It should be compactable enough to produce less-friable tablets.

It should has good flow since it improve the flow ability of the total blend.

Selection of super-disintegrates

The ideal superdisintegrant should have [45]

Poor solubility.

Poor gel formation.

Good hydration capacity.

Good moulding and flow properties

No tendency to form complexes with thedrugs.

Good mouth feel.

It should also be compatible with the otherExcipients And have desirable tableting properties

CHALLANGES IN THE PRODUCT DESIGN, FORMULATION AND MANUFACTURE OF ODTs:

- Palatability: As most of the drugs are unpalatable, orally disintegrating drug delivery systems usually contain the medicament in a taste masked form. Delivery systems disintegrate or dissolve in patient's oral cavity, thus releasing the active ingredients which come in contact with the taste buds; hence taste masking of drugs become critical to patient compliance [46][47].
- Mechanical strength: In order to allow ODTs to disintegrate in the oral cavity, they are made of either very porous and soft-moulded matrices or compressed into tablets with very low compression force, which makes the tablets friable and/or brittle, difficult to handle, and often requiring specialized peel-off blister packing that may add to the cost. Only few technologies can produce tablets that are sufficiently hard and durable to allow them to be packaged in multidose bottles, such as Wowtab® by Yamanouchi-Shaklee, and Durasolv® by CIMA labs[48][49].

- Amount of drug: Application of technologies used for ODTs is limited by the amount of drug that can be incorporated into each unit dose. In case of Lyophilized dosage forms, drug dose must be less than 400mg – insoluble drugs less than 60mg -- soluble drugs. This parameter is particularly challenging when formulating a fast-dissolving oral films [47][50].
- Hygroscopicity: Several orally disintegrating dosage forms are hygroscopic and cannot maintain physical integrity under normal conditions of temperature and humidity. Hence, they need protection from humidity which calls for specialized product packaging [51].
- Size of tablet: The degree of ease when taking a tablet depends on its size. It has been reported that the easiest size of tablet to swallow is 7-8 mm. While the easiest size to handle was one larger than 8 mm. Therefore, the tablet size that is both easy to take and easy to handle is difficult to achieve [52].
- Aqueous solubility: Water soluble drugs pose various formulation challenges because they form eutectic mixtures, which result in freezing point depression and the formation of a glassy solid that may collapse upon drying because loss of supporting structure during the sublimation process. This collapse can be prevented by using various matrix-forming excipients like Mannitol which induces crystallinity and hence impart rigidity to the amorphous composite [53][54].

CRITERIA FOR EXCIPIENT USED IN FORMULATION OF ODTs:

It must be able to disintegrate quickly.

Their individual properties should not affect the ODTs.

It should not have any interaction with drugand other excipients.

It should not interfere in the efficacy and organoleptic properties of the product.

When selecting binder (a single or combination of binders) care must be taken in the final integrity and stability of the product.

The melting point of the excipients used should be in the range of 30-35°C.

The binder may be in liquid, semi solid, solid or polymeric in nature [47][55].

EXCIPIENTS USED IN ODT's PREPARATION:

Excipients used in ODTs contain at least one superdisintegrant, diluents, a lubricant and optionally a swelling agent, a permeabilizing agent, sweeteners and flavorings.

Table1: Name and weight percentage of various excipients [56]

Name of the Excipients	% used
Superdisintegrants	1-15%
Binders	5-10%
Antistatic agent	0-10%
Diluents	0-85%

- SUPER DISINTEGRANTS:As day's passes, demand for faster disintegrating formulation is increased. So, pharmacist needs to formulate disintegrates i.e. Superdisintegrants which are effective at low concentration and have greater disintegrating efficiency and they are more effective intragranularly. This superdisintegrants act by swelling and 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[57][58].

Table2: List of Superdisintegrants [62]

Superdisintegrants	Example	Mechanism Of Action	Special comment
Crosscarmelose® Ac-Di-Sol® Nymce ZSX® Primellose® Solutab® Vivasol® L-HPC	Crosslinked cellulose	-Swells 4-8 folds in < 10 seconds. -Swelling and Wicking both.	-Swells in two dimensions. -Direct compression or granulation -Starch free
Crospovidone 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

- **BULKING MATERIALS:** Bulking materials are significant in the formulation of fast-dissolving tablets. The material contributes functions of a diluents, filler and cost reducer. Bulking agents improve the textural

characteristics that in turn enhance the disintegration in the mouth, besides adding bulk also reduces the concentration of the active in the composition. The recommended bulking agents for this delivery system should be more sugar-based such as mannitol, polydextrose, lactitol, DCL (direct compressible lactose) and starch hydrolystate for higher aqueous solubility and good sensory perception. Mannitol in particular has high aqueous solubility and good sensory perception. Bulking agents are added in the range of 10 percent to about 90 percent by weight of the final composition.

- **LUBRICANTS:** Though not essential excipients can further assistin making these tablets more palatable after theydisintegrate in the mouth. Lubricants removegrittiness and assist in the drug transportMechanism from the mouth down into the stomach.
- **TASTE MASKING:** The materials for taste-masking purpose have often been classified depending upon the basictaste. Flavoring and perfuming agents can be obtained from either natural or synthetic sources.
- Natural products include fruit juices, aromatic oils such as peppermint and lemon oils, herbs, spices, and distilled fractions of these. They are available as concentrated extracts, alcoholic or aqueous solutions, syrups, or spirit. Apart from these conventional materials, many compositions have been found to show effective taste-masking abilities with improved flavor such as alkaline earth oxide, alkaline earth hydroxide, or an alkaline hydroxide. Another composition includes phosphorylated amino acid such as phosphotyrosine, phosphoserine, and phosphothreonine and mixtures thereof. Anethole effectively masked bitter taste as well as the aftertaste of zinc, which is used in treating the common cold. Clove oil and calcium carbonate, which has been found to be particularly useful to mask the unpalatable active in formulations which are intended to be chewed or dissolve in mouth prior to ingestion in solution[59][60].
- **EMULSIFYING AGENT:** Emulsifying agents are important excipients for formulating fast-melting tablets they aid in rapid disintegration and drug release without chewing, swallowing or drinking water. In addition, incorporating emulsifying agents is useful in stabilizing the immiscible blends and enhancing bioavailability. A wide range of emulsifiers is recommended for fast dissolving tablet formulation, including alkyl sulfates, propyleneglycol esters, lecithin, sucrose esters and others.
- These agents can be incorporated in the range of 0.05 percent to about 15 percent by weight of the final composition [61].

ADVANCEMENTS IN ODT TECHNOLOGIES: [63][64]

Patented and recent advancements in ODT technology are listed in table.

EVALUATION:

The mixture of powder was evaluated for bulk density, tapped density, Carr's index, Hausner's ratio and angle of repose. The tablets were evaluated for thickness, hardness, friability, weight variation test, drug content and In-Vitro release rate studies [66][67].

1. General Appearance:The general appearance of a tablet, its visual identity and over all "elegance" is essential for consumer acceptance and tablet's size, shape, colour, presence or absence of an odour,Taste, surface texture, physical flaws and consistency and legibility of any identifying marking.
2. Size and Shape:The size and shape of the tablet can be dimensionally described, monitored and controlled.
3. Tablet thickness:Tablet thickness can be measured using a simple procedure. Five tablets are taken and their thickness is measured using Vernier Caliper[71].
4. Weight variation: 20 tablets were selected randomly from the lot and weighted individually to check for weight variation. Weight variation specification as per I.P.[68]

Table 3: Weight variation specification as per I.P[74][76]

Average Weight of Tablet	% Deviation
80 mg or less	±10
80 mg to 250 mg	±7.5
250 mg or more	±5

5. Hardness: The fracture strength, which is defined as the force required to breaking a tablet by radial compression is measured with a tablet hardness tester (Monsanto hardness tester). It is expressed in kg/cm2[69].
6. Friability: The friability of sample of six tablets is measured using a Roche Friabilator. This device subject the tablets to the combined effect of abrasion and shock in a plastic chamber revolving at 25 rpm and dropping the tablets at a height of 6 inches in each revolution. Six pre-weight tablets are rotated at 25 rpm for 4 minutes. The tablets are then reweighed after removal of fines using 60 mesh screens and the percentage of weight loss is calculated [70].

   % Friability = (Loss in weight /Initial weight) ×100

7. Wetting time: Wetting time of dosage form is related to the contact angle. It needs to be assessed to give an insight into the disintegration properties of the tablets; a lower wetting time implies a quicker disintegration of the tablet. For this purpose, a tablet is placed on a piece of tissue paper folded twice and kept in a small Petri dish (ID = 6.5 cm) containing 6 ml of water, and the time for complete wetting is measured [71].
8. Disintegration Time: The test was carried out on 6 tablets using the apparatus specified in I.P.-1996 distilled water at 37°C ± 2°C was used as a disintegration media and the time in second taken for complete disintegration of the tablet with no palatable mass remaining in the apparatus was measured in seconds 28.

   Modified Disintegration Test: 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 time for FDT needs to be modified as disintegration is required without water, thus the test should mimic disintegration in salivary contents. For this purpose, a petridish (10 cmdiameter) was filled with 10 ml of water. The tablet was carefully put in the center of petridish and the time for the tablet to completely disintegrate into fine particles was noted [75].
9. In-Vitro Dispersion Time Test: To determine dispersion time 10 ml measuring cylinder was taken in which 6 ml distilled water was added and tablet was dropped in it. Time required for complete dispersion was determined [76].
10. Dissolution test: The development of dissolution methods for ODTs is comparable to the approach taken for conventional tablets, and is practically identical. Dissolution conditions for drugs listed in a pharmacopoeia monograph, is a good place to start with scouting runs for a bioequivalent ODT. Other media such as 0.1 M HCl and buffer (pH 4.5 and 6.8) should be evaluated for ODT much in the same way as their ordinary tablet counterparts. It has been suggested that USP 2 paddle apparatus is the most suitable and common choice for orally disintegrating tablets, with a paddle speed of 50 rpm commonly used [77].
11. In vivo clinical studies: In vivo studies show the actual action of ODT in the oral-oesophageal tract, their pharmacokinetic and therapeutic efficacy, and acceptability. The investigation using gammascintigraphy showed that the dissolution and buccal clearance of fast disintegrating dosage form is rapid. The oesophageal transit time and stomach emptying time are comparable to those of traditional dosage forms i.e. tablets, capsules, or liquid forms [78][79].
12. Disintegration in oral cavity: The time required for complete disintegration of tablets in mouth is obtained from six healthy volunteers, who have given tablets from optimum formulation [80].
13. Accelerated stability study: The Orally disintegrating tablets are packed in suitable packaging and stored under the following condition for a period as prescribed by ICH guideline for accelerated studies.
    (1) 40 ± 10C
    (2) 50 ± 10C
    (3) 37 ± 10C and Relative Humidity = 75%± 5%

The tablets are withdrawn after a period of 15days and analyzed for physical characterization (Visual defects, Hardness, Friability, Disintegration, and Dissolution etc.)and drug content. The data obtained is fitted into first order

equation to determine the kinetics of degradation. Accelerated stability data are plotting according Arrhenius equation to determine the self life at 25 ^{0}C [81].

CONCLUSIONS:

Nowadays these tablets are gaining more importance in industry targeting pediatrics, geriatrics and all age groups. The ODTs have potential advantages over conventional dosage forms, with their improved patient compliance; convenience, bioavailability and rapid onset of action had drawn the attention of many manufactures over a decade. .Though considerable research has been done in the formulation development and technologies for FDTs, more intensive investigations are to be carried out in this promising area to result in newer cost effective technologies and better products. The basic approach followed by all the available ODTs technologies is to maximize the porous structure of tablet matrix to achieve rapid tablet disintegration in the oral cavity along with good taste-masking properties and excellent mechanical strength.

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