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ORODISPERSIBLE TABLETS: DEVELOPMENT, TECHNOLOGIES AND EVALUATION: AN OVERVIEW

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ABSTRACT

An orodispersible tablet or orally disintegrating tablets (ODT) is a drug dosage form developed to facilitate ease of medication and the field has become a rapidly growing area in the pharmaceutical industry. They are designed to be dissolved on the tongue rather than swallowed whole. In addition, orodispersible or orally disintegrating tablet (ODT) serve as an alternative dosage form for patients who experience dysphagia (difficulty in swallowing) in paediatrics and geriatric patients . Such formulation provide an opportunity for product line extension in the many elderly person who have difficulties in taking conventional oral dosage form (viz., solution, suspension ,tablets, and capsules) because of hand tremor and dysphagia. Other groups that may experience problems using conventional oral dosage form include the mentally ill, developmentally disabled, and patients who are uncooperative, on reduced liquid-intake plans, or are nauseated. Further, drugs exhibiting satisfactory absorption from the oral mucosa or intended for immediate pharmacological action can be advantageously formulated in these dosage forms which dissolve rapidly in saliva without chewing and additional water. Taste masking of active ingredients becomes essential in these system because the drug is entirely released in mouth. This review article summarizes the various technologies; Direct compression, freeze drying, molding, sublimation and nanonization developed for ODT and evaluation methods for tablets by employing; In-vitro disintegration test, water absorption ratio, hardness, friability and in-vitro dissolution test. Apart from these methods this review also focuses on the challenges in formulation and suitability of drug candidates for orodispersible tablets.

Key Words: Oral dispersible tablet (ODT), Drug delivery system, Conventional techniques

INTRODUCTION

The concept of orally dispersible or orally disintegrating dosage form has emerged from the desire to provide patients with more conventional means of taking their medication. Interestingly, the demand for ODT has enormously increased during the last decade, particularly for geriatric and paediatric patients who experience difficulty in swallowing (dysphagia) conventional tablets and capsules. Common among all age group, dysphagia is observed in about 35% of the general population, as well as up to 60% of the elderly institutionalized population and 18-22% of all patients in long-term care facilities. An ODT offer the luxury of much more accurate dosing than the primary alternative, oral liquids. This segment of formulation is especially designed for dysphagia, geriatric, paediatric, bed-ridden, travelling and psychotic patients who are unable to swallow or refuse to swallow conventional oral formulation. During the last decades, orally disintegrating tablets (ODT) technologies that makes tablet disintegrate in the mouth without chewing and additional water intake have drawn a great attention. Orally disintegrating tablets are also referred as fast disintegrating tablets (FDT), fast melting, fast dispersing, quick dissolve, rapid melt, porous tablets, quick disintegrating tablets, and orodispersible tablets. Recently, European pharmacopoeia has used the term orodispersible tablet for tablets that disperse or disintegrate readily and within 3 minutes in the mouth before swallowing. [1-4]

Salient features of ODT:-

- 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. [10-11]

Advantages of ODT:-

- Ease of administration to patients who refuse to swallow a tablet, such as paediatric, 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 paediatrics patients.

- Ability to provide advantages of liquid medication in the form of solid preparation.
- New business opportunities: product differentiation, line extension and life-cycle management, exclusivity of the product promotion and patent-life extension. [6-9]

Disadvantages of ODT:-

- Rapid disintegrating tablets are hygroscopic in nature so must be kept at controlled environment i.e. humidity and temperature.
- For properly stabilisation 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. [12-13]

Challenges to develop ODT [5]

- Have sufficient mechanical strength
- Minimum or no residue in mouth
- Rapid disintegration of tablets
- Compatible with taste masking technology
- Not affected by drug properties
- Avoid increase in tablet size
- Good package design
- Protection from moisture
- Bioavailability
- Stability

Selection of ODT Drug Candidates

The selection of drug candidates for delivery as ODT dosage forms depend on several factor that must be considered.

- Drugs having ability to diffuse and partition into epithelium of the upper GIT (log P > 1, or preferable > 2); and those able to permeate oral mucosal tissue are considered ideal ODT formulation.
- Some drugs require controlled or sustained release are not suitable candidates for the orally disintegrating dosage forms.
- Drugs with a short half-life and frequent dosing are not suitable candidate for ODTs.
- The drugs that produce a significant amount of toxic metabolites mediated by first pass metabolism and for drugs that have a substantial fraction of absorption in the oral cavity and segments of the pre-gastric GIT.
- The drug which have significantly different pharmacokinetic profiles compared with the same dose administered in a conventional dosage form e.g. selegiline, apomorphine, buspirone etc.
- ODTs for various categories of drugs such as neuroleptics, cardiovascular agent, analgesics, antiallergic, anti-epileptics, anxiolytics, sedatives, hypnotics, diuretics, anti-parkinsonism agent, anti-bacterial agents and drugs used for erectile dysfunction have been formulated by pharmaceutical companies.
- Some drugs which are very bitter or otherwise unacceptable taste because taste masking cannot be achieved. [14-18]

Ingredients used for ODTS

The role of excipients is important in the formulation of orally disintegrating tablets. Excipients balance the properties of the actives in ODTs. The temperature of the excipients should be preferably around 30-35°C for faster disintegrating properties. This includes both the active ingredient i.e. drug and the excipients.

Ingredients and Technologies used for Formulating ODT

Ingredients and technologies used for formulating ODT are shown in table 1.

Table 1: Ingredients and technologies used for formulating ODT

Drug(s)	Ingredients used	Technology used	Disintegration time (sec)	References
Aceclofenac	SSG, CCS, Magnesium stearate, Mannitol.	Wet granulation	32	[19]
Amlodipine besylate	Plantago ovata mucilage, MCC, Magnesium stearate, Talc, Mannitol.	Direct compression	8-43	[20]
Carvedilol	Crospovidone, SSG, Lactose Monohydrate, Talc, Magnesium stearate.	Direct compression	15-25	[21]
Baclofen	CP, MCC, SSG, Magnesium stearate, Mannitol, Talc.	Direct compression	0.5-1.5	[22]
Cefixime	Crospovidone, SSG, CCS, Mannitol, MCC.	Direct compression	15-19	[23]
Diazepam	Crospovidone, MCC, CCS, SSG, Mannitol.	Direct compression	21-36	[24]
Ciprofloxacin Hcl	Isabgol powder, Adar powder, Alginic acid, Talc, Magnesium stearate.	Direct compression	50-80	[25]
Carbamazepine	CP, MCC, SSF, Mannitol.	Direct compression	15	[26]
Doxylamine succinate	CP (Kollidon CL-SF), MCC (Vivapur 102), Magnesium stearate, Lactose, Aspartame.	Direct compression	32-57	[27]
Fenofibrate	Crospovidone, Camphor, Ammonium bicarbonate,	Direct Compression	10-20	[28]

	Magnesium stearate, Mannitol,			
Famotidine	Seed powder and Mucilage powder of Plantago ovate, PVP, Aapartame, Talc.	Wet granulation	80-120	[29]
Granisetron Hcl	CP, SSG, MCC, SSF, Mannitol.	Direct compression	20	[30]
Ibuprofen	Kollidon CL (K), Explotab (E), Pearlitol SD 200, Magnesium stearate.	Wet granulation	35-70	[31]
Nimesulide	Polyethylene glycol, PVP, Mannitol.	Freeze drying	8-19	[32]
Ondansetron	SSG, MCC, CCS, Magnesium stearate, Mannitol, Sodium saccharine.	Direct compression	3-5	[33]
Olanzapine	MCC, SSG, HPC, Sodium saccharine, Magnesium stearate, Strawberry flavour.	Direct compression	< 30	[34]
Piroxicam	Isapghula husk, Cross linked tragacanth, Cassia tora, Magnesium stearate, Talc.	Direct compression	50-70	[35]
Pheniramine maleate	CCS, MCC, SSG, CP, Pregelatinized starch, Low substituted hydroxyl propyl cellulose, Mannitol.	Direct compression	20-50	[36]
Phenytoin	Sodium carboxymethyl cellulose, Gum Arabic, Magnesium stearate, Chitosan.	Wet granulation	1-3	[37]

HPMC- Hydroxy propyl methyl cellulose
MCC- Microcrystalline cellulose

CCS- Croscarmellose sodium
SSG- Sodium starch glycolate

PEG- Polyethylene glycol
PVP- Polyvinylpyrollidone

HPC- Hydroxypropylcellulose
CP- Crospovidone

SSG- Sodium stearyl fumerate

Formulation of ODT

An ODT formulation prepared by using the various available excipients which can provide good solubility by increasing the rate of disintegration and hence the dissolution. There are various excipients available with improved activity such as superdisintegrants and sugar based excipients which play the main role in ODT formulation and also other excipients such as fillers, surface active agents, lubricants, flavours and sweetners used to fulfil the other needed functions of required formulation.

Superdisintegrants

Disintegrants are substances or mixture of substances added to drug formulation that facilitate the breakup or disintegration of tablet contents into smaller particle that dissolve more rapidly than in the absence of disintegrants. Superdisintegrants are used at a low level in the solid dosage form, typically 1-10% by weight relative to the total weight of the dosage unit. The addition of superdisintegrants principally affects the rate of disintegration and hence the dissolution. Examples of superdisintegrants with their characteristics; Crospovidone, microcrystalline cellulose, sodium starch glycolate, sodium carboxy methyl cellulose, pregelatinized starch, calcium carboxy methyl cellulose, and modified corn starch. Sodium starch glycolate has good flow ability than croscarmellose sodium and cross povidone is fibrous nature and highly compactable.

Selection of superdisintegrants

There are various factors which should be considered before selection of superdisintegrants.

- It should produce rapid disintegration (hydrophilic) when tablets meets saliva in the mouth.
- It should have good flow property since it improve the flow ability of total blend.
- It should be compactable enough to produce less-friable tablets.

Sugar based excipients

The use of sugar based excipients especially bulking agents like dextrose, fructose, isomalt, lactilol, maltilol, maltose, mannitol, sorbotol, starch hydrosate, polydextrose and xylitol, which display high aqueous solubility and sweetness, and hence impart taste masking property and a pleasing mouth feel. On the basis of molding and dissolution rate, sugar based excipients are classified into two types.

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.

Most commercial ODTs have been developed using mannitol as the bulk excipients of choice. Mannitol overwhelmingly preferred over lactose because of its extremely low hygroscopicity, excellent chemical and physical compatibility, good compressibility and better sweetness. These excipients under defined manufacturing condition gives a highly porous structure and friable exterior structure which helps in faster disintegration of ODT. They also provide a satisfactory mouth feel and so suitable for use in preparation of harder ODT by direct compression at low pressure.

Other excipients

Fillers: Directly compressible spray dried mannitol, sorbitol, xylitol, calcium carbonate, magnesium carbonate, calcium phosphate, calcium sulphate, pregelatinized starch,

magnesium trisilicate and aluminium hydroxide.

Surface active agents: Sodium doecyl sulphate, sodium lauryl sulphate, poly oxyethylene sorbotan fatty acid esters (tweens), sorbitan fatty acid esters (spans), poly oxyethylene stearate.

Lubricants: Stearic acid, magnesium stearate, talc, polyethylene glycol, liquid paraffin, magnesium lauryl sulphate, colloidal silicon dioxide.

Sweetners: Aspartame, sugar derivatives.

Flavours: Peppermint flavour, flavour oils and flavouring aromatic oils, peppermint oil, clove oil, anise oil, thyme oil, oil of bitter almonds. Flavouring agents include, vanilla, citus oils, fruits essences. [38-41]

Technologies used for ODT

The technologies which are commonly being used during the last few decades are summarized as: -

1. Freeze drying/ lyophilisation
2. Molding
3. Direct compression
4. Sublimation
5. Cotton candy process
6. Spray drying
7. Mass extrusion
8. Nanonization
9. Melt granulation
10. Phase transition

1. Freeze drying/ lyophilization

Lyophilization is one of the first generation technique in which water is sublimated from the product after freezing. It is a pharmaceutical technology which allows drying of heat sensitive drugs and biological at low temperature under condition that allow removal of water by sublimation. This process results in preparations, which are highly porous, with a very high specific surface area, and dissolve rapidly and show improved absorption and bioavailability. The active drug is dissolved or dispersed in an aqueous solution of a carrier/polymer. The prepared mixture is weighed and poured in the walls of preformed blister packs. The trays holding the blister packs are passed through liquid nitrogen freezing tunnel to freeze the drug solution or dispersion. Then the frozen blister packs are placed in refrigerated cabinets to continue the freeze drying. Finally the blisters are packaged and shipped. The freeze-drying technique has demonstrated improved absorption and increase in bioavailability. The major disadvantage of lyophilization technique are that it is expensive and time consuming, fragility makes conventional packaging unsuitable for these product and poor stability under stressed condition. [42-43]

2. Molding

In this method, molded tablets are prepared by using water-soluble ingredients so that the tablets dissolve completely and rapidly. The powder blend is moistened with a hydro-alcoholic solvent and is molded into tablets under pressure lower than that used in conventional tablet compression. The solvent is then removed by air-drying. These possess porous structure that enhance dissolution. Molded tablets can also be prepared by heat molding process, which involves setting of molten mass that contains a dispersed drug. The heat-molding process uses an agar solution as a binder and a blister packaging as a mold to manufacture a tablet. [44]

3. Direct compression

It is the simplest and most cost effective tablets manufacturing technique. Conventional equipment, commonly available excipients and a limited number of processing steps are involved in direct compression. This technique is now applied to the preparation of ODTs because of the availability of improved excipients especially superdisintegrants and diluents. The disintegration and dissolution of directly compressed tablets depends on single or combined effect of disintegrant, water soluble excipients and effervescent agents. Tablets size and hardness strongly affects the disintegrants efficacy. [45]

4. Sublimation

In the process of sublimation volatile ingredients are incorporated in the formulation to generate a porous matrix. Highly volatile ingredients like Ammonium bicarbonate, Ammonium carbonate, Benzoic acid, Camphor, Napthalene, Urea, Urethane and Phthalic anhydride may be compressed along with other excipients to formulate tablets. This volatile material is then removed by sublimation leaving behind a highly porous matrix. Tablets manufactured by this technique have been reported to disintegrate usually in 10-20 sec. [46]

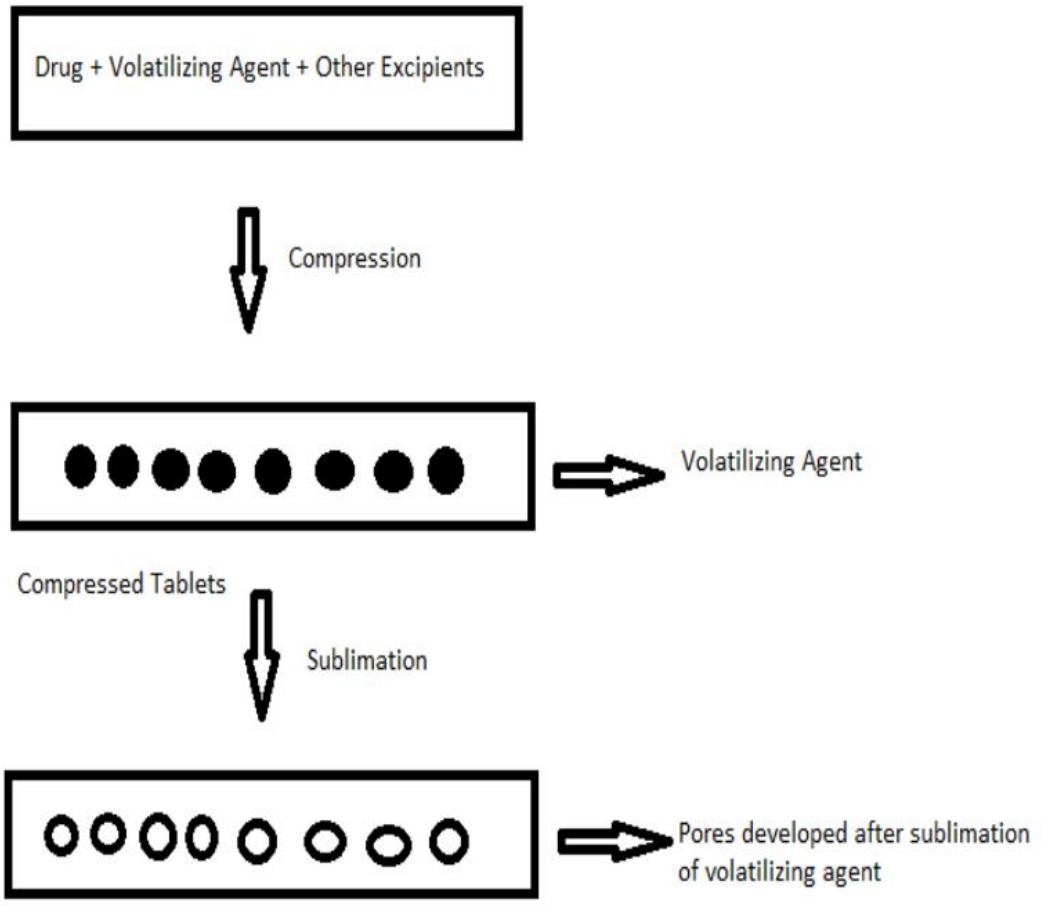

Figure 1: Steps involved in sublimation

5. Cotton candy process

This technique involves the formation of matrix of polysaccharides or saccharides by simultaneous action of flash melting and spinning. The matrix formed is partially recrystallized to have better flow properties

and compressibility. This candy floss matrix is then milled and blended with active ingredients as well as excipients and subsequently compressed to ODTs. This process can accommodate high doses of drug and offers improved mechanical strength. [47]

6. Spray drying

Spray drying can produce highly porous and spherical granules that dissolve rapidly.The formulation are incorporated by hydrolyzed and non hydrolyzed gelatin as a supporting agent and as a matrix, mannitol as a bulking agent and sodium starch glycolate or croscarmellose or crospovidone are used as superdisintegrants and an acidic material (e.g. Citric acid) and or alkali material (e.g. Sodium bicarbonate).This spray-dried powder, which compressed into tablets showed rapid disintegration and enhanced dissolution. Tablets compressed from the spray dried powder disintegrated within 20 seconds when immersed in an aqueous medium.[48]

7. Mass-Extrusion

In this method active blend is softened using the solvent mixture of water-soluble polyethylene glycol and methanol and then subsequent expulsion of softened mass through the extruder or syringe and a cylindrical shaped extrude is obtained which are cut into even segments using heated blade to form tablets. Granules of bitter drugs can be coated using this method to mask their taste .[49]

8. Nanonization

A recently developed Nanomelt technology involves reduction in the particle size of drug to nano size by wet-milling technique. The nanocrystals of the drug are stabilized against agglomeration by surface adsorption on selected stabilizer, which are then incorporated into ODTs. This technique is advantageous for the drugs which are poorly water soluble and also provide the fast disintegration/dissolution of nanoparticles leading to increased absorption and hence higher bioavailability. [50]

9. Melt granulation:-

Melt granulation is a process in which pharmaceutical powders are efficiently agglomerated by the use of binder which can be a molten liquid, a solid or a solid that melts during the process. For accomplishing this process, high shear mixer are utilized, where the product temperature is raised above the melting point of binder by a heating jacket or by the heat of friction generated by impeller blades. The main advantage of this technique as compared to conventional granulation is that no water or organic solvent is needed. This process is less time consuming as there is no drying step and uses less energy than wet granulation. [51]

10. Phase transition

It is a novel method to prepare ODTs with sufficient hardness by involving the phase transition of sugar alcohol. In this technique, ODTs prepared by compressing and subsequently heating tablets that contain two sugar alcohol, one with high and other with a low melting point.This process enhance bonding among particle leading to sufficient hardness of tablets by heating which is otherwise lacking owing to low compactibility [52].

PATENTED TECHNOLOGIE [53-57]

Now a days, there are several technologies and different processes have been developed on the basis of formulation aspects and patented by several pharmaceutical companies. Rapid-dissolving characteristic of ODTs is generally attributed to fast penetration of water into tablet matrix

resulting in its fast disintegration. These technologies are briefed or summarized in Table 2 and Table 3.

Table 2: Various patented technologies and their patent owner.

Patented technologies	Basis of technology	Patent owner	Active ingredients (Brand name)
Zydis	Lyophilization	R.P.Scherer Inc.	Loratidine (Claritin Reditab and Dimetapp Quick Dissolve)
Durasolv	Molding	Cima Labs Inc.	Hyoscyamine Sulfate (Nulev), Zolmitriptan (Zolmig ZMT)
Orasolv	Compressed Tablets	Cima Labs Inc.	Paracetamol (Tempra Quicklets), Zolmitriptan (Zolmig Repimelt)
Advatab	Microcaps and Diffuscap CR Technology	Eurand International	
Lyoc	Multiparticulate Compressed Tablets	Farmlyoc	Phloroglucinol Hydrate (Spasfon Lyoc)
Flashtab	Lyopilization	Ethypharm	Ibuprofen (Nurofen Flashtab)
Flashdose	Cotton-Candy Process	Fuisz Technology Ltd.	Tramadol Hcl (Relivia Flash dose)
Wow tab	Compressed Molded Tablets	Yamunouchi Pharma Technologies, Inc.	Famotidine (Gaster D)
Oroquick	Microcaps Taste Masking	KV Pharm.Co., Inc	Hyoscyamine Sulfate ODT
Ziplets	Molding	Eurand International	Ibuprofen (Cibalgina Due Fast)
Quicksolv	Lyophilization	Jansen Pharmaceutical	Cisapride monohydrate (Propulsid Quicksolv), Risperidone (Risperdal M-tab)

Table 3: Advantages and disadvantages of patented technologies.

Technique	Novelty	Advantages	Disadvantages
Zydis	First to market, freeze dried.	Quick dissolution, self-preserving and increased bioavailability	Expensive process, poor stability at higher temperature and humidity
Orasolv	Unique taste-masking, lightly compressed.	Taste-masking is two fold, quick dissolution.	Low mechanical strength
Flashdose	Unique spinning mechanism to produce a floss like crystalline	High surface area for dissolution.	High temperature required to melt the matrix can limit the

	structure, much like cotton candy		use of heat-sensitive drugs, sensitive to moisture and humidity
Flashtab	Compressed dosage form containing drug as microcrystals.	Only conventional tabletting technology.	_
Durasolv	Compressed dosage form, proprietary taste-masking.	Higher mechanical strength than Orasolv, good rigidity.	Inappropriate with larger dose.
Wow tab	Combination of low-mouldability and high-mouldability saccharides. Smoothmelt action gives superior mouth feel.	Adequate dissolution rate and hardness.	No significant change in bioavailability.
Ziplet	Incorporation of water-insoluble inorganic excipients for excellent physical performance.	Good mechanical strength, satisfactory properties can be obtained at high dose (450 mg) and high weight (850 mg).	As soluble component dissolves, rate of water diffusion into tablet is decreased because of formation of viscous concentrated solution.
Oraquick	Uses patented taste-masking technology.	Faster and efficient production, appropriate for heat-sensitive drugs.	_

Preformulation Studies

Bulk density

The granular powder weighing 10 gram is placed in100 ml measuring cylinder. Volume occupied by the powder was noted without disturbing the cylinder and bulk density was calculated by the following equation. [58]

$$\rho_b = M / V$$

Where: ρ_b - is bulk density, M- is the weight of powder, V- is the volume of powder.

Tapped density

Weigh 10 gram of granular powder and placed in a 100 ml measuring cylinder. The cylinder was then subjected for the fixed number of taps (≈100) until the powder bed has reached the minimum. The final volume was recorded and the tap density is calculated by following equation. [59]

$$\rho t = M / Vt$$

Compressibility index

The simplest method of measurement of free flow of powder is compressibility, an indication of the ease with which a material can be induced to flow is given by compressibility index which is calculated as follows.

$$\% C.I. = \rho t - \rho b / \rho t \times 100$$

The value below 15% indicates a powder which usually gives rise to excellent flow properties, whereas above 25% indicate poor flowability. [60]

Hausner's ratio (H)

This is an indirect index of ease of powder flow. It is calculated by the following formula.

Hausner's ratio = ρt / ρb

Where,

ρb = Bulk density

ρt = Tapped density

Lower Hausner's ratio (<1.25) indicates better flow properties than higher ones (>1.25). [61]

Porosity

Percent relative porosity (ε) is obtained using the relationship between apparent density (ρ_{app}) and true density (ρ_{true}) which was calculated by following formula. [62]

$$\varepsilon = (1 - \rho_{app} / \rho_{true}) \times 100$$

Voide volume

Voide volume (V) is obtained by difference between bulk volume (V_b) and tapped volume (V_p). Voide volume can be calculated by following formula. [63]

$$V = V_b - V$$

Angle of repose

Angle of repose was determined using funnel method. The blend is poured through a funnel that can be raised vertically until a maximum cone height (h) is obtained. Radius of the heap (r) is measured and angle of repose (θ) is calculated using following formula. [64]

$$\theta = \text{Tan}^{-1} (h / r)$$

Where,

θ = Angle of repose

h = height of the pile

r = radius of plane surface occupy by the powder

Evaluation after compression

Uniformity of weight

According to the US pharmacopoeia, weight of individual twenty tablets is recorded and then all twenty tablets are weighed together on a digital balance and the mean of tablets weight is calculated. Results are presented as mean value ± standard deviation. [65]

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/cm^2. [66]

Thickness

Tablet thickness can be measured using a simple procedure. Five tablets are taken and their thickness is measured using Vernier Caliper. [67]

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 screen and the percentage of weight loss is calculated. [68]

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

Wetting time

The wetting time of the tablets can be measured using a simple procedure. Five circular tissue papers of 10 cm diameter are placed in a petridish with a 10-cm diameter. Ten milliliters of water-soluble dye (eosin) solution is added to petridish. A tablet is carefully placed on the surface of the tissue paper. The time required for water to reach upper surface of the tablet is noted as the wetting time. [69]

Water absorption ratio

For measuring water absorption ratio the weight of the tablet of sample is noted before keeping in the petri dish containing water and then the wetted tablet is taken from the petri dish and reweighed. The water absorption ratio, R can be determined by the following equation. [70]

$$R = 100 (W_a - W_b) / W_b$$

Where,

W_a = Weight of tablet after absorption

W_b = Weight of tablet before absorption

In vitro disintegration test

The disintegration time was measured using disintegration test apparatus. One tablet is placed in each tube of the basket. This basket is immersed in water bath at 37 ^{0}C ± 2 ^{0}C. The time required for complete disintegration is recorded with standard deviation. [71]

In vitro dispersion time test

To determine dispersion time 10 mL measuring cylinder is taken in which 6 ml distilled water is added and then sample tablet is dropped in it. Time required for complete dispersion was determined. [72]

In vitro 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. [73]

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 gamma-scintigraphy 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. [74-75]

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. [76]

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 ± 1^{0}C
(2) 50 ± 1^{0}C
(3) 37 ± 1^{0}C and Relative Humidity = 75% ± 5%

The tablets are withdrawn after a period of 15 days 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. [77]

Table 4: The commercialized product of ODT available in the market are given in the table.

Brand Name	Active Drug	Pharmaceutical company
Benadryl Fastmelt	Diphehydramine	Pfizer
Benadryl Fastmely	Diphehydramine	Warner Lambert
Cibalginadue FAST	Ibuprofen	Novartis Consumer Health
Domray MD	Domperidone	Ray Remedies
Dolib MD	Rofecoxib	Panacea
Feldene melt	Piroxicam	Pfizer
Febrectol	Paracetamol	Prographarm
Imodium Instant melts	Loperamide Hcl	Janssen
Kemstro	Baclofen	Schwarz Pharma
Klonopin Wafers	Clonaxepam	Roche
Maxalt-MLT	Rizatriptan Benzoate	Merck
Mosid MT	Mosapride	Torrent
Nulev	Hyoscyamine sulfate	Schwarz Pharma
Nimulid MD	Nimesulide	Panacea
Orthoref MD	Rofecoxib	Biochem
Olanex Instab	Olanzepine	Ranbaxy
Pepcid ODT	Famotidine	Merck
Rofaday MT	Rofecoxib	Lupin
Valus	Valdecoxib	Glenmark
Zotacet MD	Cetirizine HCL	Zota Pharma
Zyprexa	Olanzapine	Eli lilly
Zofran ODT	Ondansetron	GSK
Zomig ZMT and Rapimelt	Zolmitriptan	Astra Zeneca
Claritin redi Tab	Loratidine	Schering plough Corp., USA
Olanex instab	Olanzapine	Ranbaxy lab. Ltd. New-Delhi, India
Romilast	Montelukast	Ranbaxy lab. Ltd. New-Delhi, India

Conclusion

Orally disintegrating tablets (ODT) transform into easy-to-swallow suspension on contact with the saliva, after being ingested in mouth. These are particularly useful for pediatric or geriatric patients, can be taken without liquids and facilitate treatment of emergent pain, irrespective of the place and situation where it may arise. The concept of ODT evolved to overcome some of the problems that existed in the conventional solid dosage form i.e. difficulty in swallowing of tablet in paediatric and geriatric patients who constitute a large proportion of world's population. It may lead to improve efficacy, bioavailability, rapid onset of action, better patient compliance due to its quick absorption from mouth to GIT as the saliva passes. Orally disintegrating tablet acts like solid dosage form when outside the body and solution when administered. The formulations of ODTs

obtained by some of these technologies have sufficient mechanical strength, quick disintegration/dissolution in the mouth without water. In future ODT may be most acceptable and prescribed dosage form due to its quick action. Their characteristic advantages such as administration without water, anytime, anywhere lead to their increased patient compliance in today's scenario of hectic life. Because of increased patient demand, popularity of these dosage forms will surely expand in future.

Future prospects

The innovation in the arena of formulating ODTs are aimed at both increasing the performance of the dosage form by decreasing the disintegration time and increasing the patient compliance by masking the objectionable taste of the active ingredients. To fulfil these medical needs, formulators have devoted considerable efforts to develop a novel type of dosage form for oral administration. An extension of market exclusivity, which can be provided by a fast-dissolving/disintegrating dosage form, leads to increased revenue, while also targeting underserved and under treated patient population. However, substantial amount of research remains to be conducted for the development of protein and peptide based systems that have limited bioavailability when administered by conventional tablets. Therefore in coming era, there is going to be continued interest for the development of natural polymers based orally disintegrating tablets. The future trends in the innovation of drug delivery systems will continue to bring together different technological disciplines and formulation aspects to create novel technologies.

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