



CODEN [USA]: IAJPBB

ISSN: 2349-7750

**INDO AMERICAN JOURNAL OF
PHARMACEUTICAL SCIENCES**Available online at: <http://www.iajps.com>

Review Article

ORODISPERSIBLE TABLETS:AN OVERVIEW**ANU A L*¹, SUBASH CHANDRAN M.P¹, PRASOBH G.R¹, JUNO S¹,
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Parassala, Thiruvananthapuram, Kerala, India. 695502**Abstract:**

Oral route is presently the gold standard in the pharmaceutical industry where it is regarded as the safest, most economical and most convenient method of drug delivery resulting in highest patient compliance. Oral delivery of active ingredients include a number of technologies, many of which may be classified as Orodispersible tablets (ODTs). Usually, elderly people experience difficulty in swallowing the conventional dosage forms like tablets, capsules, solutions and suspensions because of tremors of extremities and dysphagia. In some cases such as motion sickness, sudden episodes of allergic attack or coughing, and an unavailability of water, swallowing conventional tablets may be difficult. ODTs systems may offer a solution for these problems. Advancements in the technology arena for manufacturing these systems includes the use of freeze drying, cotton candy, melt extrusion, sublimation, direct compression besides the classical wet granulation processes. This has encouraged both academia and industry to generate new orally disintegrating formulations and technological approaches in this field. This article attempts at discussing the ideal characteristics, advantages and disadvantages, formulation aspects, formulation technologies and future potential of ODTs.

Keywords: Formulation technologies, Orodispersible tablets, Superdisintegrant.

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Please cite this article in press Anu A L et al., **Orodispersible Tablets:An Overview.**, Indo Am. J. P. Sci, 2019;
06(10).

INTRODUCTION:

Oral drug delivery remains the most preferred route for administration of various therapeutic agents. Recent advances in technology prompted researchers and scientists to develop oral disintegrating tablets (ODTs) with improved patient convenience and compliance. 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. 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. The United States Pharmacopoeia has also approved these dosage forms as orodispersible tablets[1]. Thus, orodispersible tablets are solid unit dosage forms like conventional tablets, but are composed of super disintegrants, which help them to dissolve the tablets within a minute in the mouth in the presence of saliva without any difficulty of swallowing. 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. The target populations for ODTs are pediatric, geriatric, and bedridden or developmentally disabled patients. Patients with persistent nausea, who are traveling, or who have little or no access to water are also good candidates[2]. The performance of ODTs depends on the technology used in their manufacture. The orally disintegrating property of these tablets is attributable to the quick ingress of water into the tablet matrix, which creates porous structure and results in rapid disintegration. Hence, the basic approaches to develop ODTs include maximizing the porous structure of the tablet matrix, incorporating the appropriate disintegrating agent and using highly water-soluble excipients in the formulation[3].

Advantages Of Odt's

- Administration to the patients who cannot swallow, such as the elderly, stroke victims, bedridden patients, patients affected by renal failure and patients who refuse to swallow such as pediatric, geriatric and psychiatric patients.
- Rapid drug therapy intervention.
- Achieve increased bioavailability/rapid absorption through pre-gastric absorption of

drugs from mouth, pharynx and oesophagus as saliva passes down[4].

- Convenient for administration and patient compliant for disabled, bedridden patients and for travelers and busy people, who do not always have access to water.
- Good mouth feel property helps to change the perception of medication as bitter pill particularly in pediatric patients.

Disadvantages Of Fast Dissolving Tablets

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

Characteristics Of An Ideal Orodispersible Tablets

Orally disintegrating drug delivery system should possess following characteristics:

- Utilizes cost effective production method.
- Require no water for oral administration[5].
- Dissolve / disperse/ disintegrate in mouth in a matter of seconds.
- Have a pleasing mouth feel and taste masking.
- Less friable and have sufficient hardness.
- Leave minimal or no residue in mouth after administration.
- Manufacturing using conventional manufacturing method.

Drug selection criteria[6]

The ideal characteristics of a drug for

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

CHALLENGES IN FORMULATION OF ODTs**1. Disintegration time and mechanical strength**

ODTs are formulated to obtain disintegration time usually less than a minute. While doing so,

maintaining a good mechanical strength is a prime challenge. Many ODTs are fragile and there are chances that such fragile tablet will break during packing, transport or handling by the patients. Tablets based on technologies like Zydis need special type of packaging. It is very natural that increasing the mechanical strength will delay the disintegration time. So a good compromise between these two parameters is always essential[8].

2. Taste masking

Many drugs are bitter in taste. A tablet of bitter drug dissolving/ disintegration in mouth will seriously affect patient compliance and acceptance for the dosage form. So effective taste masking of the bitter drugs must be done so that the taste of the drug is not felt in the oral cavity. Number of techniques are developed for masking the bitter taste of most of the drugs, that includes formation of pellets by extrusion, spheronization or mass extrusion[14], coating of drug using a taste masking polymer [9] spray drying the drug dispersed in a polymeric solution[10], complexation of drug by inclusion in cyclodextrin, drug-resinate complex formation, microencapsulation of drug by polymer[13].

Chandira R.M et al. enhanced solubility of carvedilol by β - cyclodextrin as a complexing agent[14]. Solubility studies were performed to investigate the drug carrier interaction. I.R. and D.S.C studies carried out to investigate any interaction and stability of formulation. Tablets were prepared by direct compression technique. Prepared tablets were evaluated for thickness, uniformity of weight, hardness, friability, wetting time, in-vitro disintegration time, drug content and in vitro drug release. It can be concluded that Carvedilol can be successfully complexed with Beta-cyclodextrin to prepare fast dissolving tablets in the ratio of 1: 4 .

3. Sensitivity to environmental conditions

ODTs generally should exhibit low sensitivity to environment conditions such as humidity and temperature as most of the materials used in ODTs are meant to dissolve in minimum quantity of water[15].

4. Mouth feel

ODTs should not disintegrate into larger particles in the oral cavity. The particles generated after disintegration of the ODTs should be as small as possible. ODTs should leave minimal or no residue in mouth after oral administration. Moreover addition of flavours and cooling agents like menthol improve the mouth feel[16].

5. Cost

The technology used for ODTs should be

acceptable in terms of cost of the final product. Methods like Zydis and Orasolv that require special technologies and specific packaging increase the cost to a remarkable extent.

TECHNIQUES USED IN PREPARATION OF ODTs

1. Freeze drying/ Lyophilization

Lyophilization means drying at low temperature under condition that involves the removal of water by sublimation. Drug in a water soluble matrix which is then freeze dried to give highly porous structure. The tablets prepared by lyophilization disintegrate rapidly in less than 5 seconds due to quick penetration of saliva in pores when placed in the oral cavity. Lyophilization is useful for heat sensitive drugs i.e. thermo-labile substances[17]. Freeze drying process normally consists of three steps: Material is frozen to bring it below the eutectic point. Primary drying to reduce the moisture around 4% w/w of dry product. Secondary drying to reduce the bound moisture up to required final volume[18].

Advantages: More rapid dissolution than other available solid products.

Disadvantages: High cost of the equipments & lack of physical resistance in blister packs. Ahmed I.S. et al prepared ODTs by freeze-drying an aqueous dispersion of Nimesulide containing a matrix former, a sugar alcohol, and a collapse protectant. Development of a lyophilized orally disintegrating tablet (ODT) enhanced the in vitro dissolution and in vivo absorption of Nimesulide, a drug with poor solubility and poor bioavailability. Bhojar P.K. et al formulated rapid disintegrating tablet in the blister packs using Freeze Drying Method. Eudragit EPO polymer was used for complexation with drug Trimetazidine HCl for overcoming taste problem. The Lyophilization method was used to form the drug polymer complex in a tablet. 1:3 ratio of the drug to polymer was effectively masked the bitter taste of drug[19].

2. Spray drying

This technique is based on a particulate support matrix, which is prepared by spray drying an aqueous composition containing support matrix and other components to form a highly porous and fine powder.

This then mixed with active ingredients and compressed into tablets[20]. The formulations are incorporated by hydrolyzed and non hydrolyzed gelatins as supporting agents, mannitol as bulking agent, sodium starch glycolate or crosscarmellose sodium as disintegrating and an acidic material (e.g. citric acid) and / or alkali material (e.g. sodium bicarbonate) to enhance disintegration and

dissolution. Tablet compressed from the spray dried powder disintegrated within 20 seconds when immersed in an aqueous medium[21]

Advantages:

Rapid disintegration of tablets. Masareddy R29 et al studied the effect of co-processed excipient bases in formulation of orodispersible tizanidine HCl tablets by direct compression method. Co-processed excipient of microcrystalline cellulose with SSLhydroxypropylcellulose was prepared using spray drier in 1:1, 1:2 and 1:3 ratio. Formulated tablets were evaluated for hardness, friability, *in vitro* disintegration time and *in vitro* drug release. Granules obtained by spray drying technique were found to be more spherical which improved its flow property and was supported by scanning electron microscope studies. Inclusion of coprocessed excipient base in formulation of Orodispersible tablets enhanced disintegration significantly[22].

3. Molding

Tablets prepared by this method are solid dispersions. Molded tablets offer improved taste due to watersoluble sugars present in dispersion matrix. Molding process is of two type's i.e. solvent method and heat method. Solvent method involves moistening the powder blend with a hydro alcoholic solvent followed by compression at low pressures in molded plates to form a wetted mass (compression molding). The solvent is then removed by air-drying[23]. The tablets manufactured in this manner are less compact than compressed tablets and possess a porous structure that hastens dissolution. The heat molding process involves preparation of a suspension that contains a drug, agar and sugar (e.g. mannitol or lactose) and pouring the suspension in the blister packaging wells, solidifying the agar at the room temperature to form a jelly and drying at 30°C under vacuum[24].

Advantages: Moulded tablets disintegrate more rapidly and offer improved taste because the dispersion matrix is, in general made from water soluble sugars.

Disadvantages: Moulded tablets do not possess great mechanical strength. Erosion & breakage occur during handling & opening of blister packages.

4. Sublimation

In this method a subliming material like (Ammonium bicarbonate, Ammonium carbonate, Urea, Benzoic acid, Naphthalene, camphor) is removed by sublimation from compressed tablets and high porosity is achieved due to the formation of many pores. where camphor particles previously

existed in the compressed tablets prior to sublimation of the camphor[25]. A high porosity was achieved due to the formation of many pores where camphor particles previously existed in the compressed mannitol tablets prior to sublimation of the camphor. These compressed tablets which have high porosity (approximately 30%) rapidly dissolved within 15 seconds in saliva.

Advantage: Tablets dissolve in 10-20 sec. and exhibit sufficient mechanical strength. Kumar R et al. developed FDT with improved Haloperidol dissolution by sublimation of tablets containing camphor as subliming agent. Orodispersible tablets of haloperidol were prepared by wet granulation technique using camphor as subliming agent and sodium starch glycolate together with croscarmellose sodium as superdisintegrants. Camphor was sublimed from the granules by exposing the granules to vacuum. The porous granules were then compressed in to tablets. Alternatively, tablets were first prepared and later exposed to vacuum. Sublimation of camphor from tablets resulted in superior tablets as compared with the tablets prepared from granules that were exposed to vacuum[26]. The results revealed that the tablets containing subliming agent had a good dissolution profile.

5. Mass Extrusion

This technology involves softening of the active blend using the solvent mixture of water soluble polyethylene glycol and methanol and expulsion of softened mass through the extruder or syringe to get a cylindrical shaped extrude which are finally cut into even segments using heated blade to form tablets. This process can also be used to coat granules of bitter drugs to mask their taste.

Advantage: Mask bitter taste by coating the granules. Mansing G. Patil et al[34] prepared orally disintegrating tablets of Tramadol hydrochloride for achievement of quick onset of action of the drug. An attempt was to prepare bitterless orally disintegrating tablet using Eudragit E 100 as a taste masking agent. Mass extrusion was the technique used for preparing taste masked granules and tablet was prepared using superdisintegrants like crospovidone, Croscarmellose sodium and sodium starch glycolate. The extrusion technique represents a novel application of polymer processing technology to prepare pharmaceutical dosage forms. The process involves embedding a drug in a polymeric carrier while shaping the composite material to form a pharmaceutical product. The drug release from orally disintegrating tablets increased with increasing concentration of superdisintegrants and was found to be highest with formulations containing Crospovidone.

6. Direct Compression

Direct compression represents the simplest and most cost effective tablet manufacturing technique. This technique can now be applied to:

a) Superdisintegrants:

In many orally disintegrating tablet technologies based on direct compression, the addition of superdisintegrants principally affects the rate of disintegration and hence the dissolution. The presence of other formulation ingredients such as water-soluble excipients and effervescent agents further hastens the process of disintegration. For the success of fast dissolving tablet, the tablet having quick dissolving property which is achieved by using the super disintegrants.

MECHANISMS OF SUPERDISINTEGRANTS

There are four major mechanisms for tablet disintegration as follows:

1) Swelling

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

2) Porosity and capillary action (wicking):

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

3) Due to particle-particle repulsive forces:

The electric repulsive forces b/w particles responsible for disintegration. It is secondary to wicking.

4) Due to deformation:

During tab. compression, disintegrated particles gets deformed and in contact with aq. media returns to normal structure (inc. in size).

Eg: starch.

7. Phase transition process

Kuno *et al* proposed a novel method to prepare ODTs with sufficient hardness by involving the phase transition of sugar alcohol. In this technique, ODT were 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. Heating process enhances the bonding among particles leading to sufficient hardness of tablets which was otherwise lacking owing to low/little compactibility[27].

IMPORTANT PATENTED TECHNOLOGIES IN ODTs

1. Zydis

ZYDIS® (R.P. Scherer, Swindon, UK), using freeze drying processes, is one of the first generations of fast disintegrating dosage forms. There are approximately 12 marketed ZYDIS® products, including lorazepam, piroxicam, loperamide, loratidine, enalapril. This drug delivery system consists of freeze-dried tablets having active drug designed to rapidly disintegrate in the mouth. The freeze-dried tablet is made by lyophilizing a suspension or solution of drug containing various excipients such as polymer, polysaccharides, preservatives, pH adjusters, flavors, sweeteners, and colors, which is then filled in blisters. Freeze drying occurs in the blisters, which are then sealed and further packaged. Some of the advantages of the Zydis system include fast disintegration time. Some of the disadvantages include low throughput, high cost of goods, and limited taste masking.

2. OraSolv, DuraSolv, and PakSolv

OraSolv and DuraSolv are CIMA's core ODT tablet based technologies. The ingredients contained in the technology include polyols as fillers, disintegrant, which may include an effervescence couple, flavor, sweetener, and lubricant. The drug may be taste masked if required typically utilizing a fluid bed coating process. The tableting process includes direct compression, and can accommodate a wide range of potency from less than 1 mg to as high as 500 mg. Tablets manufactured with OraSolv technology should contain an effervescence couple along with microparticles of drug within a rupturable coat. The tablets manufactured are compressed at a low hardness that promotes fast disintegration. The dosage forms need to be packaged in foil-foil aluminum blisters with a dome shape that impact physical protection and impermeability to moisture. This constitutes the PakSolv Technology. PakSolv is a "domeshaped" blister package that prevents the vertical movement of the tablet within the depressions, because the diameter of the lower portion of the dome is too narrow to accommodate the tablet. PakSolv also offers light, moisture, and child resistance. Tablets manufactured with DuraSolv technology contain a non-directly compressible filler and a lubricant. They may or may not contain effervescence, and the drug need not be taste masked. DuraSolv tablets are compressed at higher hardness compared to OraSolv that allows for packaging in bottles or push through blisters[28].

Advantage: low cost of goods, standard manufacturing technology, standard packaging

format and materials, and low development costs and risks.

Disadvantage: slightly longer disintegration time.

3. Lyoc

Lyoc technology is owned by Cephalon Corporation. CIMA is a subsidiary of Cephalon, and currently manages the Lyoc R&D efforts. This was the first freeze-drying-based technology introduced for ODTs. The process involves preparation of a liquid solution or suspension of the drug containing fillers, thickening agents, surfactants, non-volatile flavoring agents, and sweeteners. This homogenous liquid is then deposited in blister cavities and subjected to freeze drying.

Advantage: compared to other freeze-dried dosage forms include absence of preservatives.

4. Flashtab

Flashtab tablet matrix consists of a swellable agent (modified starch or microcrystalline cellulose) and a super disintegrant (croscopolidone or croscarmellose). The system may also contain, depending on the need, a highly water-soluble polyol with binding properties such as mannitol, sorbitol, maltitol, or xylitol, instead of the swellable agent as mentioned before. The active is taste masked by direct coating. Tablets manufactured using this technology produce durable tablets in which the excipients are first granulated using wet or dry granulation process, then the coated drug is mixed with the excipient granules and compressed into tablets that can be handled and packaged using conventional processing equipment. Tablets for blister packaging can withstand the pressure used to push the tablet out of the lidding foil of the blister card. Tablets containing hygroscopic material can also be blister packaged, by using high-quality polyvinyl chloride or aluminum foils, which provide a higher degree of moisture protection than ordinary polyvinyl chloride or polypropylene foils.

5. Flash Dose

Fuisz technologies was the inventor of the Flash Dose technology. It is now owned by Biovail. Flash Dose tablets are manufactured utilizing SHEARFORM matrix in which material containing substantial amounts of fibrous polysaccharides, which are processed by simultaneous action of flash melting and centrifugal force, are compressed to form fine sugar fibers. Flash Dose tablets containing a matrix of these sugar fibers disintegrates very rapidly upon contact with saliva, with disintegration times of a few seconds. The tablets produced by FlashDose are hydrophilic and highly porous, owing to relatively low compression

during the pressing of the tablets. For taste masking, Fuisz uses its own patented, single-step, solvent-free process, termed "CEFORMTM technology," which produces uniform microspheres with a very narrow particle size distribution. The resulting tablets produced by this process are soft, friable, and highly moisture sensitive. They require specialized packaging materials and processes to protect them from external humidity and mechanical abrasion.

6. Wow tab

Wow tab technology is patented by Yamanouchi Pharmaceutical Co. WOW means "Without Water". In this process, combination of low mouldability saccharides with hardness 0-2 kg and high mouldability saccharides with hardness more than 2 kg is used to obtain a rapidly melting strong tablet. The active ingredient is mixed with a low mouldability saccharide e.g. lactose, glucose, and mannitol and granulated with a high mouldability saccharide

e.g. Maltose, Oligosaccharides and compressed into tablet.

7. Pharmaburst technology

Pharmaburst™ is a "Quick Dissolve" delivery system patented by SPI Pharma. Pharmaburst is a co-processed excipient system which involves a dry blend of a drug, flavors, and lubricant then followed by compression into tablets which then dissolve within 30-40 seconds. Tablets manufactured by this methodology have sufficient strength can be packed in blister packs and bottles.

8. Frosta™

Akina owns Frosta technology. The technology incorporates manufacture of highly plastic granules using a plastic material, a material enhancing water penetration, and a wet binder. These granules can then be compressed into tablets at low pressure, thus enabling fast disintegration upon administration. The tablets obtained have excellent hardness and rapid disintegration time ranging from 15 to then this solution is frozen. At the temperature the first solvent will remain in the solid form, and then the frozen solution contacts the second solvent which is usually, ethanol, menthol, or acetone. Thus, the first solvent is removed after a few hours of contacting the second solvent to result in a usable matrix. The final product disintegrates almost instantly [29]. This method is claimed to prevent or to reduce the incidence of cracking during the final preparation, having uniform porosity and also the adequate strength for handling.

9. Quicksolv technology

Quicksolv (Janssen Pharmaceutica, Beese,

Belgium). In the Quicksolv formulation, the matrix compositions are dissolved in the solvent (usually water), and hazardous drugs. As manufacturing losses are negligible, this process is useful for small quantities of drug.

10. Nanocrystal technology

This is patented by Elan, King of Prussia. Nanocrystal technology includes lyophilization of colloidal dispersions of drug substance and water-soluble ingredients filled in to blister pockets. This method avoids manufacturing process such as granulation, blending, and tableting, which is more advantageous for highly potent and hazardous drugs. As manufacturing losses are negligible, this 30 sec depending on size of tablet.

11. ZiPLETS/advatab

This technology is patented by Pessano con Bornago, Italy. It utilizes water-insoluble ingredient combined with one or more effective disintegrants to produce ODT with improved mechanical strength and optimal disintegration time at low compression force. This technology handles high drug loading and coated drug particles and does not require special packaging, so they can be packed in push through blisters or bottles.

PREFORMULATION STUDIES

Angle of Repose, Bulk Density, Tapped Density, Void Volume, Porosity, Compressibility characteristics (Carr's and Hausner index).

1) Angle of Repose:

The angle of repose was determined by the funnel method suggested by Newman. The accurately weighed blend was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of blend. The drug blend was allowed to flow through the funnel freely on to the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation:

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

$$\text{Therefore } \theta = \tan^{-1} h/r$$

Where: θ = Angle of repose, h = height of the cone
r = Radius of the cone base

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

Table 1: Angle of Repose as an Indication of Powder Flow Properties

Sr. No.	Angle of Repose	Type of Flow
1	<20	Excellent
2	20-30	Good
3	30-34	Passable
4	>34	Very poor

2) Bulk Density:

Specific bulk volume or reciprocal of bulk density is called bulkiness or bulk. Bulkiness increases with a decrease in particle. The bulkiness can be calculated by the following formula,

$$\text{Bulkiness} = 1/Db$$

Where, Db = Bulk Density.

Bulk density is defined as the mass of the powder divided by the bulk volume and is expressed as gm/cm³. The bulk density of a powder primarily depends on particle size distribution, particle shape and the tendency of particles to adhere together. The particles are pack in such a way so as to leave large gaps between their surfaces resulting up in light powder of low bulk density. Bulk density is very important in the size of containers needed for handling, shipping, and storage of raw material and blend. It is also important in size blending equipment.

$$Db = M/Vb$$

Where, Db = Bulk Density

M = Weight of sample in gm

Vb = Bulk volume (untapped volume)

3) Tapped Density

It is the ratio of total mass of the powder to the tapped volume of the powder. Volume was measured by tapping the powder for 750 times and the tapped volume was noted if the difference between these two volumes is less than 2%. If it is more than 2%, tapping is continued for 1250 times and tapped volume was noted. Tapping was continued until the difference between successive volumes is less than 2 % (in a bulk density apparatus). It is expressed in g/ml and is given by

$$Dt = M / Vt$$

Where, M is the mass of powder

Vt is the tapped volume of the powder.

4) Void Volume

The volume of the spaces is known as the void volume "v" and is given by the Formula,

$$V = Vb - Vt$$

Where, Vb = Bulk volume (volume before tapping)

Vt = True volume (volume after tapping)

5) Porosity

The porosity ϵ 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

$$\epsilon = \frac{V_b - V_t}{V_b} = 1 - \frac{V_t}{V_b}$$

Porosity is frequently expressed in percentage and is given as

$$\% \epsilon = (1 - \frac{V_t}{V_b}) \times 100.$$

6) Carr's index (or) % compressibility

It indicates powder flow properties. It is expressed in percentage and is given by

$$I = \frac{D_t - D_b}{D_t} \times 100$$

$$I = \frac{D_t - D_b}{D_t} \times 100$$

Dt

Where, Dt is the tapped density of the powder and Db is the bulk density of the powder. If the bed of particles is more compressible the blend will be less flowable.

7) 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 following formula:

$$\text{Hausner ratio} = \frac{D_t}{D_b}$$

Where, Dt is the tapped density.

Db is the bulk density.

Hausner's ratio <1.25 – Good flow = 20% compressibility index

1.25 – Poor flow = 33% compressibility index

8) Identification of drug sample

It was confirmed by melting point determination and also by FT-IR spectral analysis.

9) Drug excipient Compatibility study:

Compatibility of the drug with excipients was determined by FT-IR spectral analysis, this study was carried out to detect any changes on chemical constitution of the drug after combined it with the excipients. The samples were taken for FT-IR study.

EVALUATION OF ORODISPERSIBLE TABLETS

Evaluation parameters of tablets mentioned in the Pharmacopoeias need to be assessed, along with some special tests are discussed here.

1. Hardness

A significant strength of ODT is difficult to achieve due to the specialized processes and ingredients used in the manufacturing. The limit of hardness for the ODT is usually kept in a lower range to facilitate early disintegration in the mouth.

The hardness of the tablet may be measured using conventional hardness test [29,30].

2. Friability

To achieve % friability within limits for an ODT is a challenge for a formulator since all methods of manufacturing of ODT are responsible for increasing the % friability values. Thus, it is necessary that this parameter should be evaluated and the results are within bound limits (0.1-0.9%).

3. Tablet thickness

Tablet thickness is an important characteristic in reproducing appearance and also in counting by using filling equipment. Some filling equipment utilizes the uniform thickness of the tablets as a counting mechanism. Thickness was recorded using vernier calliper.

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. is shown in Table 3.

Table 2: Weight Variation Specification as per IP

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

3. Wetting time and water absorption ratio

Wetting time of dosage form is related to with the contact angle. Wetting time of the ODT is another important parameter, which needs to be assessed to give an insight into the disintegration properties of the tablet. Lower wetting time implies a quicker disintegration of the tablet. The wetting time of the tablets can be measured by using the simple procedure. Five circular tissue papers of 10cm diameter are placed in a petridish. Ten milliliters of water soluble dye 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. For measuring water absorption ratio the weight of the tablet before keeping in the petridish is noted (Wb). The wetted tablet from the petridish is taken and reweighed (Wa). The water absorption ratio, R can be the determined according to the following equation.

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

4. Moisture uptake studies

Moisture uptake studies for ODT should be conducted to assess the stability of the formulation. Ten tablets from each formulation were kept in a dessicator over calcium chloride at 37°C for 24h.

The tablets were then weighed and exposed to 75% relative humidity, at room temperature for 2 weeks. Required humidity was achieved by keeping saturated sodium chloride solution at the bottom of the dessicator for 3 days. One tablet as control (without super disintegrants) was kept to assess the moisture uptake due to other excipients. Tablets were weighed and the percentage increase in weight was recorded.

5. Disintegration test

The time for disintegration of ODTs is generally <1min and actual the disintegration time that patients can experience ranges from 5 to 30s. The standard procedure of performing disintegration test for these dosage forms has several limitations and they do not suffice the measurement of very short disintegration times. The disintegration test for ODT should mimic disintegration in mouth with in salivary contents.

6. Dissolution test

The development of dissolution methods for ODT is comparable to approach taken for conventional

tablets and is practically identical when ODT does not utilize taste masking. Commonly the drugs may have dissolution conditions as in USP monograph. Other media such as 0.1 N HCl, pH 4.5 and pH 6.8 buffers should be used for evaluation of ODT in the same way as their ordinary tablet counterparts. Experience has indicated that USP 2 paddle apparatus is most suitable and common choice for dissolution test of ODT tablets, where a paddle speed of 50 rpm is commonly used. Typically the dissolution of ODTs is very fast when using USP monograph conditions. Hence slower paddle speeds may be utilized to obtain a comparative profile. Large tablets approaching or exceeding one gram and containing relatively dense particles may produce a mound in the dissolution vessel, which can be prevented by using higher paddle speeds. These two situations expand the suitable range of stirring to 25-75 rpm. The USP 1 (basket) apparatus may have certain applications for ODT but is used less frequently due to specific physical properties of tablets.

Table 3: ODT products in Indian market:

Brand Name	Active Ingredients	Company
Nimulid-MD	Nimesulide	Panacea Biotech
Zyrof meltab	Rofecoxib	Zydus Cadila
MOSID-MD	Mosapride Citrate	Torrent Pharmaceuticals
Feledine Melt	Piroxicam	Pfizer
Maxalt ODT	Famotidine	Merck
Remeron Sol Tab	Mirtazapine	Organon
Romilast	Montelukast	Ranbaxy
Manza BDT	Olanzapine	Orchid
Olanexinstab	Olanzapine	Ranbaxy
Valus	Valdecoxib	Glenmark
Torrox MT	Rofecoxib	Torrent
Rofaday MT	Rofecoxib	Lupin

Future of ODTs:

ODT technology is applicable to a wide range of therapeutic agents including generics, thereby adding value, i.e. "supergenerics" for veterinary or human application. Some new quality control methods can be developed to determine the technological aspects of orally disintegrating tablets to define the characteristics of ODTs. Protein and peptide-based therapeutics that used via oral route, have limited bioavailability when administered by immediate release tablets. Those kinds of products usually degrade immediately in gastrointestinal system. The developments of improved oral protein delivery Technology by ODTs, that dispersed and/or dissolved in the saliva, are very promising for the delivery of high molecular weight protein and peptide[38]. It would be an innovative improvement in the ODT technology when development of ODTs with controlled release properties that can deliver drugs which has short half-lives like 12–24 hours. The added convenience and compliance of such formulations will be used more immensely[39]. In addition, the ability to formulate drugs in large doses will bring another important technological advance. In general, the ODT formulations require large amounts of excipients, and having large doses of drug will only make the final formulation too big to handle. ODT formulations that require fewer excipients than the drug itself will be a break through[40]. ODT technologies are in progress, but development of formulation of ODTs that contains lipophilic active pharmaceutical ingredients is a challenge. New ODT technology should be developed to find a solution for this problem. As far as seen in the literature there is not much delayed release ODTs in the market. Controlled release ODTs and/or in line with the purpose system and/or fixed dose combination ODT technologies can be developed as a next generation.

CONCLUSION:

Orally disintegrating tablets have potential advantages over conventional dosage forms, with improved patient compliance, convenience, bioavailability and rapid onset of action. They are a very good alternative for drug delivery to geriatric and pediatric patients. They have significant advantages of both solid and liquid dosage forms, as they remain solid during storage, which aid in stability of dosage forms and transform into liquid form within few seconds after its administration. As a result of the variety of technologies for its formulation, several commercial products are available in the market. Thus ODT has tremendous scope for being the delivery system for most of the drugs in near future.

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