JOURNAL OF PHARMACEUTICAL SCIENCE AND BIOSCIENTIFIC RESEARCH (JPSBR)

(An International Peer Reviewed Pharmaceutical Journal that Encourages Innovation and Creativities)

Orodispersible Tablet of Proton Pump Inhibitor Drugs: A Review

Patel Poojan*, Tanwar YS, Jaimin Modi, Amit Patel

Bhupal Nobels' college of Pharmacy, Udaipur, India

ABSTRACT:

The most important drug delivery route is undoubtedly the oral route. It offers advantages of convenience of administration and potential manufacturing cost savings. Drugs that are administered orally, solid oral dosage forms in general and tablets in particular represent the preferred class of product. Today drug delivery companies are focusing on solid oral drug delivery systems that offer greater patient compliance and effective dosages. Since the development cost of a new drug molecule is very high, efforts are now being made by pharmaceutical companies to focus on the development of new drug dosage forms for existing drugs with improved safety and efficacy together with reduced dosing frequency and the production of more cost effective dosage forms**.** To fulfill these medical needs, pharmaceutical technologists have developed a novel oral dosage form known as Orally Disintegrating Tablets which disintegrate rapidly in saliva without the need to take it with water. In any solid dosage forms, an important variable is the rate at which the active substance goes into solution or dissolves to reach the systemic circulation. Dissolution of the active substance is essential for it to be absorbed through the biological membranes into systemic circulation for eliciting its desired pharmacological activity. The most important role of a drug delivery system is to get the drug "delivered" to the site of action in sufficient amount and at the appropriate rate.

Keywords: Melt in mouth tablet (MMT), orally disintegrating tablets, Proton Pump Inhibitors

Article history:
Received 6 Mar 2013
Accepted 10 April 2013
Available online 13 April 2013

For Correspondence:

Mr. Patel Poojan

Bhupal Nobels' college of Pharmacy, Udaipur,

Rajsthan, India

Email: poojanpatel50@gmail.com

INTRODUCTION:

Now a day's, there has been an enhanced demand for more patient-friendly and compliant dosage forms. As a result, the demand for developing new technologies has been increasing annually. 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**.** Drug dissolution and absorption as well as onset of clinical effect and drug bioavailability may be significantly greater than those observed from conventional dosage forms[1]**.**

Orally disintegrating tablets are also called as orodispersible tablets, quick disintegrating tablets, mouth dissolving tablets, fast disintegrating tablets, fast dissolving tablets, rapid dissolving tablets, porous tablets, and rapimelts[2].

A melt-in-mouth tablets (MMT) can be defined as a solid dosage form which when placed on tongue disintegrates rapidly, releasing the drug, which dissolves or disperses in the saliva and then swallowed[3].

Fast dispersible tablets disintegrate either rapidly in water, to form a stabilized suspension or disperse instantaneously in the mouth to be swallowed without the aid of water. There are two different types of dispersible tablets which have to be distinguished[4]: one dosage form disintegrates instantaneously directly in the mouth to be swallowed without the need for drinking water, while the other tablet formulation can readily be dispersed in water to form dispersion easy to ingest by the patient[5]. Conventional dosage form is very popular in pharmaceutical industries because of its easy transportation and low manufacturing cost.

However for pediatrics and geriatrics fast dissolving tablet is preferred due to its swallowing conveniences. Many elderly persons face difficulties in administering conventional oral dosage forms because of hand tremors and dysphagia. Swallowing problem is common in children because of their underdeveloped muscular and nervous systems. In some cases like motion sickness, sudden episodes of allergic attack or coughing and during unavailability of water, swallowing conventional tablets is difficult. To fulfill these medical needs, formulators have devoted considerable efforts for developing a novel type of dosage form for oral administration known as orally disintegrating tablets (ODT). This is an innovative technology where the dosage form containing active pharmaceutical ingredients disintegrates rapidly usually in a matter of seconds without the need for water, providing optimal convenience to the patient. Innovators and inventor companies have given these tablets various names such as mouth dissolving, fast melting, fast dissolving or orodisperse. The European Pharmacopoeia defines orodispersible tablet that can be placed in the mouth where it disperses rapidly before swallowing[6].

ADVANTAGES OF ORODISPERSIBLE TABLETS

- Administration to the patients who cannot swallow, such as the elderly, stroke victims, bedridden patients, patients affected by renal failure & patients who refuse to swallow such as pediatric, geriatric & psychiatric patients[7].
- Rapid drug therapy intervention.
- Achieve increased bioavailability/rapid absorption through pregastric absorption of drugs from mouth, pharynx and oesophagus as saliva passes down.
- 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.
- The risk of chocking or suffocation during oral administration of conventional formulations due to physical obstruction is avoided, thus providing improved safety.
- New business opportunity like product differentiation, product promotion, patent extension and life cycle management[8,9].
- Convenience of administration and accurate dosing as compared to liquid
- Benefit of liquid medication in the form of solid preparation.
- More rapid drug absorption from the pre-gastric area i.e. mouth, pharynx and oesophagus which may produce rapid onset of action.
- Pregastric absorption can result in improved bioavailability, reduced dose and improved clinical performance by reducing side effects.
- Improved patient compliance.
- Suitable during traveling where water is may not be available.
- No specific packaging required, it can be packaged in push through blisters.
- Good chemical stability as conventional oral solid dosage form.

IDEAL PROPERTIES OF ORODISPERSIBLE TABLETS

- Not require water to swallow and should dissolve or disintegrate in the mouth within a few seconds[10].
- Allow high drug loading.
- Be compatible with taste masking and other excipients.
- Have a pleasing mouth feel.
- Leave minimal or no residue in the mouth after oral administration.
- Have sufficient strength to withstand the rigors of the manufacturing process and post manufacturing handling.
- Exhibit low sensitivity to environmental conditions such as humidity and temperature.
- Be adaptable and amenable to existing processing and packaging machinery.
- Allow the manufacture of tablets using conventional processing and packaging equipments at low cost[11,12].

PHATHOLOGY OF ORODISPERSIBLE TABLETS

Peptic Ulcer

A peptic ulcer is a hole in the gut lining of the stomach, duodenum, or esophagus. A peptic ulcer of the stomach is called a gastric ulcer; of the duodenum, a duodenal ulcer; and of the esophagus, an esophageal ulcer. An ulcer occurs when the lining of these organs is corroded by the acidic digestive juices which are secreted by the stomach cells[13].

H. pyloriare the major factor in the development of gastritis and ulcers. NSAIDs (Nonsteroidal Anti-Inflammatory Drugs) including aspirin and cigarette smoking are also an important cause of ulcer formation. Symptoms include minimal indigestion or no discomfort, upper abdominal burning or hunger pain one to three hours after meals and in the middle of the night. Proton pump inhibitors are used to treat different kinds of peptic ulcer.

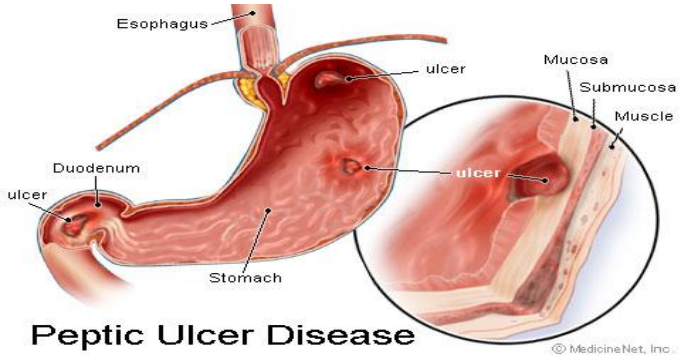


Figure: 2 Peptic ulcer disease

Proton-Pump Inhibitors (PPI'S)

According to the Biopharmaceutical Classification System (BCS), drug substances are classified as follows:

Class I - High Permeability, High Solubility.
Class II - High Permeability, Low Solubility.
Class III - Low Permeability, High Solubility.
Class IV - Low Permeability, Low Solubility.

Class I drugs are likely to exhibit few bioavailability problems.

Class II drugs are prone to dissolution rate– limited absorption.

Class III drugs are likely to exhibit permeation rate–limited absorption.

Class IV drugs may present serious obstacles to oral bioavailability and some may be best formulated in a solubilized form such as a liquid filled or semisolid-filled capsule. Proton pump inhibitors (PPI), substituted benzimidazoles, which inhibit the final common step in gastric acid secretion.

The key action mechanism of the PPI's is inhibition of H^+/K^+- adenosine triphosphate (also known as acid pump or proton pump), an enzyme present in the gastric parietal cells. This effect on the final step of the gastric acid formation thereby reducing gastric acid output both during basal conditions and simulated acid secretion, irrespective of stimulus[14,15].

Reflux oesophagitis, duodenal ulcer, gastric ulcer, NSAID associated gastric and duodenal ulcers or erosions, acid related dyspepsia, Gastroesophageal reflux disease. Stress-related or drug-induced erosive gastritis, esophageal refluxes are the various ailments where treatment with esomeprazole proves to be appropriate. Group of proton pump inhibitors includes derivatives of benzimidazole, like omeprazole, lansoprazole, pantoprazole, rabeprazole, etc.

Absorption of the most PPI's takes place in the proximal small intestine. All PPI's are extensively protein-bound and all undergo hepatic metabolism. All of the currently available delayed-release proton pump inhibitors have a short elimination half-life ($t_{1/2}$) of between 1 and 2 hours. Aside from bioavailability in the first few days of oral dosing, there are no substantive differences among currently available delayed release PPI's with respect to pharmacokinetics.

Challenges in the formulation of odts

Mechanical strength and disintegration time: 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 many 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[16].

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.

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

Sensitivity to environmental conditions: ODT generally should exhibit low sensitivity to environment conditions such as humidity and temperature as most of the materials used in an ODT are meant to dissolve in minimum quantity of water.

Cost: The technology used for an ODT 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[17].

Various technologies used in the manufacture of odts

The fast-dissolving property of the MDTs is attributed to quick ingress of water into tablet matrix resulting in rapid disintegration. Hence, the basic approaches to develop MDTs include:

- Maximizing the porous structure of the tablet matrix.
- Incorporating the appropriate disintegrating agent/agents.
- Using highly water-soluble excipients in the formulation.

So far, several techniques have been developed on the basis of different principles. The resulting dosage forms vary on grounds like

- Mechanical strength of the final product
- Drug and dosage form stability
- Mouth feel
- Taste
- Rate of dissolution and absorption from saliva
- Swallow ability and overall bioavailability

The various technologies are developed for the preparation of Orally Disintegrating Drug Delivery System that are:

1. Freeze drying, Spray drying
2. Molding
3. Phase transition process
4. Melt granulation
5. Sublimation
6. Mass Extrusion
7. Cotton Candy Process
8. Direct compression

Freeze drying or Lyophilization

Lyophilization is a process in which water is sublimated from the product after freezing. Lyophilization is a pharmaceutical technology which allows drying of heat sensitive drugs and biological at low temperature under conditions that allow removal of water by sublimation. Lyophilization results in preparations, which are highly porous, with a very high specific surface area, which dissolve rapidly and show improved absorption and bioavailability[18].

Freeze-drying allows immediate dissolution of the tablets because of their high porosity, and enhances drug stability, especially for moisture-sensitive substances; on the other hand, a porous network is associated with low physical resistance and high friability. Special packaging is required in some cases.

A typical procedure involved in the manufacturing of ODT using this technique is mentioned here. The active drug is dissolved or dispersed in an aqueous solution of a carrier/polymer. This mixture is poured into the wells of the 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. After freeze-drying the aluminium foil backing is applied on a blister-sealing machine. Finally the blisters are packaged and shipped.

MDTs manufactured using lyophilization process, usually contain excipients like polymers (e.g., gelatin, alginates and dextrin) to provide strength and rigidity to tablets; polysaccharides (e.g., mannitol and sorbitol) to impart crystallinity and hardness to the matrix and to improve palatability; collapse protectants (e.g., glycine) to prevent the product from shrinking in its packaging during manufacturing or storage; flocculating agents (e.g., xanthan gum and acacia) to provide uniform dispersion of drug particles; preservatives (e.g., parabens) to prevent microbial growth; permeation enhancers (e.g., sodium lauryl sulfate) to improve transmucosal permeability; pH adjusters (e.g. citric acid etc.) to optimize chemical stability; flavors and sweeteners to improve patient compliance and water to ensure formation of porous units.

Advantages

The major advantage of using this technique is that the tablets produced by this technology have very low disintegration time and have great mouthfeel due to fast melting effect.

Disadvantage

The major disadvantages of lyophillization technique are that it is expensive and time consuming; fragility makes conventional packaging unsuitable for these products and poor stability under stressed conditions.

Spray drying

Spray drying is used in pharmaceutical industries to produce highly porous powders. The processing solvent is evaporated rapidly by spray drying, which renders the product highly porous and thus can be used in manufacturing ODT.

In this technique, gelatin can be used as a supporting agent and as a matrix, mannitol as a bulking agent and sodium starch glycolate or crosscarmellose or crospovidone are used as superdisintegrants. Tablets manufactured from the spray-dried powder have been reported to disintegrate in less than 20 seconds in aqueous medium.

Allen and Wanghave reported this technique for preparing fast dissolving tablets. The formulation contained bulking agent like mannitol and lactose, a superdisintegrant like sodium starch glycolate and crosscarmellose sodium and acidic ingredient (citric acid) and/or alkaline ingredients (e.g. sodium bicarbonate). This spray-dried powder, which compressed into tablets showed rapid disintegration and enhanced dissolution[19].

Molding

The preparation of ODT using molding technology employs water-soluble ingredients so that the tablet dissolves completely and rapidly. The active ingredients in most cases are absorbed through the mucosal lining of the mouth.

Different molding techniques can be used to prepare mouth-dissolving tablets:

A. Compression molding: The manufacturing process involves moistening the powder blend with a hydro-alcoholic solvent followed by compressing into mold plates to form a wetted mass which is then air dried to remove the solvent. Such tablets are less compact than compressed tablets and possess a porous structure that hastens dissolution.

B. Heat molding: A molten matrix in which drug is dissolved or dispersed can be directly molded into orodispersible tablets. The tablets prepared using heat molding process involves settling of molten mass that contain a dispersed or dissolved drug. In this process, the suspension or solution of drug, agar and sugar is prepared and then poured into the blister packaging. The agar solution is then solidified at room temperature to form a jelly and dried at 30$^{°C}$ under the vacuum. Developed orally disintegrating tablets was found to improve the mouth feel due to the presence of the water soluble sugars.

C. No vacuum lyophilization: This process involves evaporation of solvent from a drug solution or suspension at a standard pressure.

Molded tablets had less mechanical strength. Drug can be present as micro particles or discrete particles dispersed in the matrix. However, adding sucrose, acacia or polyvinyl pyrrolidone can increase mechanical strength. They possess highly porous structure which is supposed to increase their disintegration and dissolution rates.

Advantages

As the dispersion matrix is made from water-soluble sugars, moulded tablets disintegrate more rapidly and offer improved taste. These properties are enhanced when tablets with porous structures are produced or when components that are physically modified by the moulding process are used. In comparison to lyophilization process, tablets produced by moulding technique are easier to adapt to the industrial scale.

Disadvantage

As the moulded tablets have poor mechanical strength, they may undergo erosion and breaking during handling. Though hardening can increase the strength of the tablets but it would be at the cost of their disintegration time.

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 FDTs without any special apparatus. FDT 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. The increase of tablet hardness with heating and storage did not depend on the crystal state of the lower melting point sugar alcohol[20].

The combination of low and high melting point sugar alcohols, as well as a phase transition in the manufacturing process is important for making orally disintegrating tablets without any special apparatus. Here, tablet produced by compressing the powder containing two sugar alcohols of high and low melting point and subsequently heating at temperature between their two melting points. Orally disintegrating tablets 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. The increase of tablet hardness with heating and storage did not depend on the crystal state of the lower melting point sugar alcohol.

Kuno et al. studied the effect of preparation method on the properties of orally disintegrating tablets manufactured using phase transition of sugar alcohol.

Before heating process, tablet did not have sufficient hardness because of low compatibility but after heating, increase in interparticular bonding or binding surface area occurs which then increased tablet hardness.

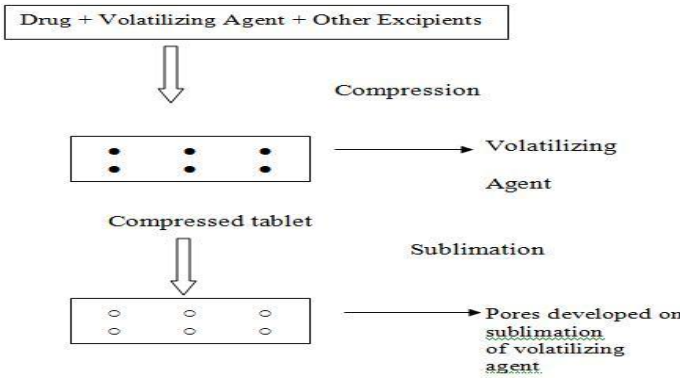
Melt granulation

Abdelbary et al. prepared orally disintegrating tablet by incorporating a hydrophilic waxy binder PEG 6-stearate (Superpolystate®) in the formulation. It has melting point of 33-37$^{°C}$ and HLB value of 9. It acts as a binder and increases the physical resistance of tablet. It helps for fast disintegration of tablet when place in mouth and leaving no residue in oral cavity. Perissutti et al. developed the orally disintegrating tablets of carbamazepine by melt granulation technique. The granules were prepared by using polyethylene glycol (PEG-4000) as a melting binder and lactose monohydrate as hydrophilic filler without using solvents or water. The dissolution profiles of granules containing crospovidone as an intragranulating agent were found to be superimposable to those prepared without it. Also, the extragranular addition of a small amount of crospovidone gave rise to a further increase in disintegration rate and dissolution performances[21].

Sublimation

The key to rapid disintegration of ODT is preparation of a porous structure in the tablet matrix. To generate such a porous matrix, volatile ingredients are incorporated in the formulation that is later subjected to a process of sublimation.

Highly volatile ingredients like ammonium bicarbonate, ammonium carbonate, benzoic acid, camphor, naphthalene, urea, urethane and phthalic anhydride may be compressed along with other excipients into a tablet. This volatile material is then removed by sublimation leaving behind a highly porous matrix. Tablets manufactured by this technique have reported to usually disintegrate in 10-20 sec. Even solvents like cyclohexane, benzene can be used as pore forming agents.



Vacuum drying technique has been very often used by researchers to sublime the volatile ingredients and thus maximize the porous structure in the tablet matrix. It is likely that a porous hydrophilic matrix will easily pick up the disintegrating medium and break quickly.

Koizumi et al. prepared highly porous compressed tablets. They used mannitol as a tablet matrix material while camphor as subliming agent. Camphor was removed by subliming in vacuum at 800^{oC} for 30 minutes to develop pores in the tablets[22].

Makino et al. described a method of producing a fast dissolving tablet using water as a pore forming material. They used a mixture containing active ingredient and carbohydrates (glucose, mannitol, xylitol etc) which then moistened with water (1-3% w/w) and compressed into tablets. Then water was removed, yielding highly porous tablet.

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[23].

Cotton Candy Process

This process utilizes a unique spinning mechanism to produce floss-like crystalline structure. Cotton candy process involves formation of matrix of polysaccharides or saccharides by simultaneous action of flash melting and spinning. The matrix formed is partially recrystallized to improve flow property and compressibility. This candy floss matrix is then milled and blended with active ingredients and excipients and subsequently compressed to orally disintegrating tablet. This process can accommodate larger drug doses offers improved mechanical strength. However, high-process temperature limits the use of this process[24].

Direct compression

Direct compression represents the simplest and most cost effective tablet manufacturing technique. This technique can now be applied to preparation of FDT because of the availability of improved excipient especially superdisintegrant & sugar based excipient.

(A) Superdisintegrant:

In many orally disintegrating tablet technologies based on direct compression, the addition of superdisintegrant principally affects the rate of disintegration and hence the dissolution. The presence of other formulation ingredients such as water-soluble excipient and effervescent agents further hastens the process of disintegration. Bi et al and Wantanbe et alhave used microcrystalline cellulose (MCC) and low substituted hydroxyl propyl cellulose (HPC) to manufacture FDT[25]. The ratio of MCC to HPC varied from 8:2 to 9:1. It and Sugiharainvestigated use of agar powder as a disintegrant because the powder absorbs water and swells without forming gel at physiological temperature. Ethylpharm (France) has introduced a Flash dose technology, which contains coated crystals and micro granules along with the disintegrant. In this technology, two types of granules are used; a disintegrating agent (e.g. modified cellulose-crosscarmellose) which has a high swelling force, and a swelling agent (e.g. starch) which has a low swelling force[26].

Shirwaikar and coworkers prepared atenolol tablets by dry granulation method using three superdisintegrant, crosscarmellose sodium (Ac-Di-Sol), crospovidone and sodium starch glycolate, and they found that Ac-Di-Sol was the best superdisintegrant among the three.

(B**) Sugar Based Excipients:**

This is another approach to manufacture FDT by direct compression. The use of sugar based excipient especially bulking agents like dextrose, fructose, isomalt, lactilol, maltilol, maltose, mannitol, sorbitol, starch hydrolysate, polydextrose and xylitol, which display high aqueous solubility and sweetness, and hence impart taste masking property and a pleasing mouth feel[27].

FDT formulators prefer to use a directly compressible mannitol, which enables the preparation of robust tablets that can withstand processing and transportation. Specially textured directly compressible, spray-dried or granulated mannitol excipient has been designed to meet these needs. These excipient under defined manufacturing conditions gives a highly porous structure and friable exterior structure which helps in faster disintegration of FDT, they also provide a

satisfactory mouth feel and so suitable for use in preparation of harder FDT by direct compression at low pressure.

Nanonization

A recently developed Nanomelt technology involves reduction in the particle size of drug to nanosize by milling the drug using a proprietary wet-milling technique. The nanocrystals 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[28]. Other advantages of this technology include fast disintegration/dissolution of nanoparticles leading to increased absorption and hence higher bioavailability and reduction in dose, cost effective manufacturing process, conventional packaging due to exceptional durability and wide range of doses (up to 200 mg of drug per unit).

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, carboxy methylcellulose, hydroxypropyl methylcellulose, hydroxyl ethylcellulose, 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 microparticles of the drug can be incorporated into the film[29,30]. This film, when placed in mouth, melts or dissolves rapidly, releasing the drug in solution or suspension form. The features of this system include paper thin films of size less than 2X2 inches, dissolution in 5 sec, instant drug delivery and flavoured after taste.

Evaluation of orodispersible tablet

Tablets from all the formulation were subjected to following quality control test.

General Appearance

The general appearance of a tablet, its visual identity and over all "elegance" is essential for consumer acceptance. Include in are tablet's size, shape, color, presence or absence of an odour, taste, surface texture, physical flaws and consistency and legibility of any identifying marking[31].

Size and Shape

The size and shape of the tablet can be dimensionally described, monitored and controlled[32].

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. Ten tablets were taken and their thickness was recorded using micrometer[33].

Uniformity of weight

I.P. procedure for uniformity of weight was followed, twenty tablets were taken and their weight was determined individually and collectively on a digital weighing balance. The average weight of one tablet was determined from the collective weight. The weight variation test would be a satisfactory method of determining the drug content uniformity.

Table 1: Tablet uniformity of weight

Average weight of tablets (mg)	Maximum percentage deviation
130 or less	10
130-324	7.5
More than 324	5

Tablet hardness

Tablet hardness is measured with hardness testers like Monsanto. A tablet is placed in the hardness tester and load required to crush the tablet is measured. The hardness of MDTs is generally kept lower than conventional tablets as increased hardness delays the disintegration of the tablet. A good compromise between mechanical strength and disintegration time is achieved for a satisfactory mouth dissolving formulation[34].

Friability

It is measured of mechanical strength of tablets. Roche friabalator was used to determine the friability by following procedure. A preweighed tablet was placed in the friabalator. Friabalator consist of a plastic-chamber that revolves at 25 rpm, dropping those tablets at a distance of 6 inches with each revolution. The tablets were rotated in the friabalator for at least 4 minutes. At the end of test tablets were de-dusted and reweighed, the loss in the weight of tablet is the measure of friability and is expressed in percentage as

$$\% \text{ Friability } = \frac{\text{loss in weight}}{\text{initial weight}} \text{ x } 100$$

***In vitro* Dispersion Time**

Disintegration or more specifically dispersion times were measured in 900 ml purified water according to the I.P. method without disc at room temperature (25°C ± 2°C). The disintegration times of 6 individual tablets were recorded and the average DT was noted**.**

Wetting time

A conventional method was used to measure wetting time and capillarity of the orodispersible tablets. The tablet was placed in a petridish of 5.5 cm in diameter, containing 10 ml of water at room temperature and the time for complete wetting was recorded. To check for reproducibility, the measurements were carried out six times and the tablet was mean value calculated[35].

Water Absorption Ratio

A piece of tissue paper folded twice was placed in a small petridish (10 cm diameter) containing 6 ml of water. A tablet was put on the tissue paper and allowed to wet completely. The wetted tablet was then reweighed. Water absorption ratio, R was determined using following equation,

$$R = 100 \times \frac{Wa - Wb}{Wb}$$

Where, W_a = weight of tablet after water absorption
W_b = weight of tablet before water absorption.

Moisture uptake

Moisture uptake studies for FDT should be conducted to have an insight into the stability of the formulation. Ten tablets from each formulation were kept in desiccators over calcium chloride at 37˚C for 24 h. The tablets were then weight and exposed to 75% RH, at room temperature for two weeks[36,37]. Required humidity was achieved by keeping saturated sodium chloride solution at the bottom of the desiccators for three days. One tablet as control (without superdisintegrant) was kept to assess the moisture uptake due to other excipient. Tablets were weighed and the percentage increase in weight was recorded.

Stability testing of drug (temperature dependent stability studies)

The fast dissolving tablets are packed in suitable packaging and stored under the following conditions for a period as prescribed by ICH guidelines for accelerated studies[38].

(I) 40 ± 1 °C
(II) 50 ± 1°c
(III) 37 ±1 ° C and RH 75% ± 5%
The tablets were withdrawn after a period of 15 days and analyzed for physical characterization (Visual defects, Hardness, Friability, Disintegrations, and Dissolution etc.) and drug content. The data obtained is fitted into first order equations to determine the kinetics of degradation. Accelerated stability data are plotting according Arrhenius equation to determine the shelf life at 25 ° C.

REFERENCES:

1. Hirani JJ, Rathod DA, Vadalia KR. Orally Disintegrating Tablets: A Review. Trop J Pharm Res. 2009;8:161-72.
2. Bharawaj S, Jain V, Sharma S, Jat RC, Jain S. Orally Disintegrating Tablets: A Review. Drug Invention Today. 2010;2:81-8.
3. Bandari S, Mittapalli RK, Gannu R, Rao YM. Orodispersible tablets: An overview. Asian J Pharm. 2008:2-11.
4. Jha SK, Vijayalakshmi P, Karki R, Goli D. Formulation and evaluation of melt-in-mouth tablets of haloperidol. Asian J Pharm. 2008:225-60.
5. Schiermeierc S, Schmidt PC. Fast dispersible ibuprofen tablets. Eur J Pharm Sci 2002;15:295–305.
6. Parakh SR, Gothoskar AV. A review of mouth dissolving tablet technologies. Pharm Tech. 2003;27:92-8.
7. Chien YW. Potential Developments and new approaches in oral controlled release drug delivery system. 1985:1294-1330.
8. Chien YW. Rate controlled drug delivery system controlled release Vs sustained release medical program technology. 1987:15-21.
9. Brahmankar PM, Jaiswal SB. Biopharmaceutics and pharmacokinetic A treatise. 9th ed. 2000. p. 1-3.
10. Bradoo R. Fast Dissolving Drug Delivery Systems. J Am Med Asso. 2001;4:27-31.
11. Parakh SR, Gothoskar AV. A review of mouth dissolving tablet technologies. Pharma technol. 2003;27:92-100.
12. Kuchekar BS, Atul CB, Mahajan HS. Mouth dissolving tablets: a novel drug delivery system. Pharma Times. 2003;35:7-9.
13. Kuno Y, Kojima M, Ando S, Nakagami H. Evaluation of rapidly disintegrating tablets manufactured by phase transition of sugar alcohols, Journal of Controlled Release. 2005;105(1):16-22.
14. Kuno Y, Kojima M, Ando S, Nakagami H. Effect of preparation method on properties of orally disintegrating tablets made by phase transition. Int J Pharm. 2008;355:87–92.
15. Abdelbary G, Prinderre P, Eouani C, Joachim J, Reynier JP, Piccerelle PH. The preparation of orally disintegrating tablets using a hydrophilic waxy binder. Int J Pharm. 2004;278:423–33.
16. Perissutti B, Rubessa F, Moneghini M, Voinovich D. Formulation design of carbamazepine fast-release tablets prepared by melt granulation technique. Int J Pharm. 2003;256:53–63.
17. Koizumi IK et al. New Method of Preparing Highly Porous Rapidly saliva Soluble Tablets by Sublimation Technique. Int J Pharm. 1997;152:127-31.

18. Makino T, Yamado M, Kikuta JI. Fast Dissolving Tablet. US patent 5,720,974;1998.
19. Bhaskaran S, Narmada GV. Rapid dissolving tablet a novel dosage form. Indian Pharmacist. 2002;1:9–12.
20. Chiver TE, Minn O. Process for making candy floss. US patent 730057;2003.
21. Bess W S, Kulkarni N, Ambike SH, Ramsay MP. Fast dissolving orally consumable solid film containing a taste masking agent and pharmaceutically active agent at weight ratio of 1:3 to 3:1. US Patent 7067116. 2006.
22. Kuchekar BS, Mahajan S, Bandhan AC. Mouth dissolving tablets of sumatriptan. Indian drug. 2004;41:592-8.
23. Lalla JK, Mamania HM. Fast dissolving rofecoxib tablets. Indian J Pharm Sci. 2004; 59(4):23-6.
24. Shahi SR, AgrawalGR, Shinde NV, Shaikh SA, Shaikh SS, SomaniVG, ShamkuvarPB, Kale MA. Formulation and *in vitro* evaluation of orodispersible tablets of etoricoxib with emphasis on comparative functionality evaluation of three classes of superdisintegrants. Rasayan J Chem. 2008;1:292-300.
25. Erlangung. Study to design stable lansoprazole pellets. Inaugural dissertation 2008.
26. Horn J. The proton-pump inhibitors: similarities and differences. Clinical therapeutics. 2000;22:266–80.
27. http: www.bailymed.nlm.nih.gov/dailymed/drugInfo.cfm?id=15904
28. Young PM. Sodium starch glycolate, In: Handbook of Pharmaceutical Excipients; Rowe RC, Sheskey PJ, Quinn ME. Published by Pharmaceutical Press and American Pharmacist Association, 2009, 6th edition, 663-6.
29. Hapgood KP, Obara S. Hydroxypropyl cellulose low substituted. In: Handbook of Pharmaceutical Excipients; Rowe RC, Sheskey PJ, Quinn ME. Published by Pharmaceutical Press and American Pharmacist Association, 2009, 6th edition, 322-4.
30. Kibbe AH.Crospovidone. In: Handbook of Pharmaceutical Excipients; Rowe RC, Sheskey PJ, Quinn ME. Published by Pharmaceutical Press and American Pharmacist Association, 2009, 6th edition, 208-10.
31. Weller PJ.Neotame. In: Handbook of Pharmaceutical Excipients; Rowe RC, Sheskey PJ, Quinn ME. Published by Pharmaceutical Press and American Pharmacist Association, 2009, 6th edition, 460-1.
32. Langdon BA, Mullarney MP.Sucralose. In: Handbook of Pharmaceutical Excipients; Rowe RC, Sheskey PJ, Quinn ME. Published by Pharmaceutical Press and American Pharmacist Association, 2009, 6th edition, 701-3.
33. Castell D, Bagin R, Goldlust B, Major J, Hepburn B. Comparison of the effects of immediate-release omeprazole powder for oral suspension and pantoprazole delayed-release tablets on nocturnal acid breakthrough in patients with symptomatic gastro-oesophageal reflux disease. Aliment Pharmacol Ther. 2005;21:1467-74.
34. Yang R, Schulman SG, Zavala PJ. Acid–base chemistry of omeprazole in aqueous solutions. Analytica Chimica Acta. 2003;481:155–164.
35. Channer KS, Virjee J. Effect of posture and drink volume on the swallowing of capsules. Br Med J. 1982;285:1702.
36. Hey H, Jorgensen F, Sorensen K, Hasselbalch H, Wamberg T. Oesophageal transit of six commonly used tablets and capsules. Br Med J. 1982;285:1717-9.
37. Tekade NP, Bhajipale NS, Ganesan V, Thenge RR, Dewade DR. Orodispersible tablets of lansoprazole: formulation,characterization and *in vitro* evaluation. 2010;2:400-5.
38. Shimizu T, Sugaya M, Nakano Y, Izutsu D, Mizukami Y, Okochi K et al. Formulation Study for Lansoprazole Fast-disintegrating Tablet. III. Design of Rapidly Disintegrating Tablets. Chem Pharm Bull.2003;51:1121-7.