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Orally disintegrating tablets: A review

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ABSTRACT

Orally Disintegrating Tablet (ODT) is such type of an innovative and unique drug delivery system which is gaining more attention and attraction in the research field of rapidly dissolving technology. ODTs are solid dosage forms containing active ingredients which dissolve or disintegrate quickly within a second, when placed on tongue. ODT technologies address the need of geriatric, pediatric and psychiatric patients who may feel difficulty in swallowing, thus ODTs are preferred alternative to conventional tablet and capsules due to better patient compliance. In the design of drug delivery system, comforts of drug administration and patient conformity have considerable prominence. They are several methods employed for preparing ODTs conventionally are spray drying, freeze drying, direct compression, melding, and sublimation while new technologies have been developed for the formulation of orodispersible tablets. This article emphasis the various aspects of ODT formulation and to review the development of ODTs, new ODT technologies and evaluation methodologies, mechanism of super disintegration, challenges faced during formulation and its limitations.

Keywords: Improved bioavailability, orally disintegrating tablets, Superdisintegrants.

INTRODUCTION

Oral administration of drugs is preferred due to its ease of swallowing, distress avoidance, versatility and most significantly, patient compliance. The large number of patients find it difficult to swallow tablets and capsules, and do not take their medicines as prescribed. The most evident drawback of the commonly used oral dosage forms like tablets and capsules is difficulty in swallowing leading to patient's incompliance particularly in case of Pediatric and geriatric patients. Pediatric patients may suffer from ingestion problems as a result of underdeveloped muscular and nervous control. Those who are travelling or have little access to water are similarly affected.[1]

The concept of Fast Dissolving Drug Delivery System emerged from the desire to provide patient with more conventional means of taking their medication. It is estimated that 50% of the population affected by this problem, which finally results in a higher chance of noncompliance and ineffective therapy[2]. Pharmaceutical technologists have developed a novel oral dosage form known as Orally Disintegrating Tablets (ODTs) which disintegrate rapidly in saliva, usually in a matter of seconds, without the need to take it water. Drug dissolution and absorption as well as onset of clinical effect and drug bioavailability may be significantly greater than those observedfrom conventional dosage forms.

A wide variety of pharmaceutical research is directed at developing new dosage forms. Most of these efforts have focused on either formulating novel drug delivery systems or increasing the patient compliance. Fast Dissolving Tablet (FDT) is the most widely preferred commercial products [3]. Fast Dissolving Tablet have major advantages that is there is no need of water for administration, rapid onset of action, reduce risk of suffocation, avoid hepatic first pass metabolism [4].

Orally disintegrating tablets are also called as orodispersible tablets, quick disintegrating tablets, mouth dissolving tablets, fast disintegrating tablets, fast dissolving tablets, porous tablets, and rapid melts. United States Pharmacopoeia has used the term orodispersible tablets that disperses readily and within 3 min in mouth before swallowing[5].Fastdissolving drug delivery system (FDDDS) is a newer concept which combinesthe advantages of both liquid and solid formulation and at the same time, offer advantages over the traditional dosage forms.

The benefits of Fast dissolving tablets are to improve patients' compliance, rapid onset of action, increased bioavailability and good stability which make these tablets popular as a in the dosage form of choice in the current market [6]. This review presented the concise information about the Fast-Dissolving Tablet (FDT). The ultimate aim of this article is to review the properties, advantages, limitations, challenges in formulation, manufacturing techniques, newer technologies and evaluation tests of ODTs.

Ideal properties of ODTs

The ideal characteristics of a drug for oral dispersible tablet include[7].

- 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 50mg.
- Short halflife 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.

Advantages of FDTs [8]

- Improved compliance.
- No water needed.
- Better taste.
- Improved stability.
- Suitable for controlled/ sustained release actives.
- Allows high drug loading
- Ability to provide advantages of liquid medication in the form of solid preparation.
- Cost effective.
- Rapid drug therapy intervention.
- High drug loading is possible.
- Have acceptable taste and pleasant mouth feeling.

Limitations [9,10]

- The tablets commonly have insufficient mechanical strength.
- The tablets may leave an unpalatable taste and grittiness in the oral cavity if not formulated properly.
- Drugs which have large doses, can cause problems to formulate them into ODTs.
- Patients who simultaneously take anti- cholinergic drugs are not suitable candidates for ODTs.

Criteria for ODTS[11, 12]

- ODT should leave minimal or no residue in mouth after oral administration, compatible with pleasing mouth feel.
- Effective taste masking technologies should be adopted for bitter taste drugs.
- Exhibit low sensitivity to environment condition such as humidity and temperature.
- ODTs should dissolve / disintegrate in the mouth in matter of seconds without water.
- Have sufficient mechanical strength and good package design.
- The drug and excipient property should not affect the orally disintegrating tablets.
- Be portable and without fragility concern

Challenges in formulating ODTS [24 -29]

Fast disintegration

ODTs shoulddisintegrate inthe mouth without the aid of water or with a very small amount of water. The "Fast disintegration" usually means disintegration of tablets in less than 1 minute, but it is preferred to have disintegration as soon as possible. The disintegration fluid is provided by the saliva of the patient.

Palatability

Oral dispersible tablets dissolve or disintegrate near the taste buds. A pleasant taste inside the mouth becomes critical for patient acceptance. Unless the drug is tasteless or does not have an undesirable taste, taste- making techniques should be used. An ideal taste- masking techniques should provide good mouth feel and should be compatible with ODT formulations. The amount of taste masking material should be as low as possible to reduce the tablet size.

Tablet strength and porosity

In order to disintegrate the oral dispersible tablet in oral cavity, the tablet structure should have a highly porous network and should use low compression force, which makes the tablets friable or brittle, which is difficult to handle. Because the strength of a tablet is related to compression pressure, it is important to find the porosity that allows fast water absorption while containing high mechanical strength.

Hygroscopicity

Generally oral dispersible tablets are hygroscopic and cannot maintain physical integrity under normal conditions of temperature and humidity. This problem can be especially challenging because many highly water-soluble excipients are used in the formulation to enhance fast dissolving properties as well as to create good mouth feel. Those highly water-soluble excipients are susceptible to moisture. Hence, they need protection from various environmental conditions.

Size of tablet

The degree of ease when taking a tablet depends on its size. It has been reported that the easiest size of tablet to swallow is 7-8 mm while the easiest size to handle was one larger than 8mm. Therefore, the tablet size that is easy to take and easy to handle is difficult to achieve.

Amount of drug

ODTs are limited by the amount of drug that can be incorporated into each unit dose. For lyophilized dosage forms, the drug dose must be lower than 400 mg for insoluble drugs and less than 60mg for soluble drugs. This parameter is particularly challenging when formulating a fast-dissolving films.

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 flavours andcooling agents like menthol improve the mouth feel.

Sensitivityto 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.

The following characteristics may render a drug unsuitable for delivery as an ODT

- These should be the characters not formulated to mouth dissolving tablets.
- Short half life
- Very bitter taste (difficult to mask)
- Required controlled or sustained release.

Development challenges of ODTS [29-31]

Because administration of MDTS is different from administration of Conventional tablets. The MDTS should maintain several unique properties.

- Fast disintegration
- Taste of active ingredients.
- Drug properties
- Solubility
- Crystal morphology
- Solubility
- Particle size
- Hygroscopicity
- Compressibility
- Bulk density
- Tablet strength and porosity
- Moisture sensitivity, MDTS should be moisture resistant.
- These water-soluble excipients are susceptible to moisture so a good package design to protect MDTS is needed.

Table 1: Challenges in formulation of ODTs[60-63]

Challenges	Description
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. It is very natural that increasing the mechanical strength will delay the disintegration time.
Taste masking	Many drugs are bitter in taste. 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 feels	Tablet should not disintegrate into larger particles in the oral cavity. The particles generated after disintegration of the tablet should be as small as possible. Tablet should leave minimal or no residue in mouth after oral administration.
Sensitivity to environment	Tablet generally should exhibit low sensitivity to environment conditions such as humidity and temperature as most of the materials used in a tablet are meant to dissolve in minimum quantity of water.
Palatability	As most drugs are unpalatable, tablets should contain the medicament in a taste- masked form.
Mechanical strength	In order to allow ODTs to disintegrate in the oral cavity, they are made of either very porous and soft-molded matrices or compressed into tablets with very low compression force, which makes the tablets friable and / or brittle, difficult to handle, and often requiring specialized peel- off blister packing that may add to the cost.
Hygroscopic property	Several orally disintegrating dosage forms are hygroscopic and cannot maintain physical integrity under normal conditions of temperature and humidity. Hence, they need protection from humidity. Hence, they need protection from humidity which calls for specialized product packaging.
Aqueous solubility	Water- soluble drugs pose various formulation challenges because they form eutectic mixtures, which result in freezing – point depression and the formation of a glassy solid that may collapse upon drying because of loss of supporting during the sublimation process.
Size of tablet	It has been reported that the easiest size of tablet is to swallow is 7-8 mm while the easiest size to handle was one larger than 8 mm.
Fast Disintegration	FDTs should disintegrate in the mouth additional water or with a very small amount of water.

Technologies used for manufacturing of orally disintegrating tablets

Various processes employed in formulating ODTs including conventional technologies and patented technologies. It includes,

Spray drying

Spray drying is a process by which highly porous, fine powders can be produced. Spray- dryers are invariably used in the pharmaceutical industry to produce highly porous powders. Spray drying provides a rapid and economically efficient way to eliminate solvents and produces highly porous and fine powders. The formulations are compounded by hydrolysed and non-hydrolysed gelatine as supporting agents, mannitol as bulking agent, croscarmellose sodium or sodium starch glycolate as disintegrating agent. To enhance disintegration and dissolution by adding appropriate acidic or alkaline material. Allen et al. have reported applying this process to the production of Fast dissolving tablets[13]. The formulation was spray dried to yield a porous powder.

Freeze drying or lyophilization

Lyophilization process involves removal of solvents from a frozen drug solution or a suspension containing structure-forming excipients. The disintegration and dissolution properties are enhanced by the desired properties of tablets that have very light and highly porousstructures. A process in which water is sublimated from the product after freezing. The drying process may give rise to the glassy amorphous structure of excipients and drug substance [14]. Jaccard and Leyder used lyophilization to create an oral pharmaceutical preparation that not only dissolves rapidly but also improved the bioavailability of several drugs such as spironolactone and oleandomycin [15].

Sublimation

Compressed tablet which contains highly water-soluble components can show slow dissolution behaviour, due to the low porosity of the tablets that reduces water penetration into the matrix. When inert volatile solid ingredients like ammonium bicarbonate, ammonium carbonate, benzoic acid, camphor, hexamethylene tetramine, naphthalene, phthalic anhydride were added to along with other tablet excipients and the blend was compressed in to table, which are finally subjected to a process of sublimation resulting in highly porous structures. Sublimation temperature ranged from 40 °C to 60° C[16].

Molding

Melded tablets are made up of water-soluble ingredients. The powder mixture is sprinkled with a solvent. The mixture is melded into tablets under pressure. Applied pressure should be lower than those used in conventional tablet compression. Creation of highly porous structure at a low pressure to improve dissolution. This process is also known as Compression Moldings. The tablet produced by meldingare solid dispersion. Melded tablets disintegrate more rapidly and offer improved taste because the dispersion matrix is in general made from water soluble sugars. The active ingredients in most cases are absorbed through the mucosal lining of the mouth. Unfortunately, moulded tablets do not possess higher mechanical strength.[17]

Mass extrusion

The mass extrusion 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 cylinder of the product into even segments using heated blade to form tablets. The dried cylinder can also be used to coat granules of bitter tasting drugs and thereby masking their bitter taste. [18, 19]

Direct compression

It is cost effective and easiest manufacturing process. This technique is now commonly used to improve the availability of improved tablet excipients, especially disintegrating agents and sugar-based excipients. Tablets obtained by conventional compression method are less friable, but disintegrate very slowly. Usually, wet granulation technique is considered to be convenient and cost-effective way to formulate ODTs. [20, 21]

Patented technologies for preparation of ODTS

Many patented technologies are available for preparing mouth dissolving tablets. They are:

Zydis technology[32-36]

Zaydi's formulation is a unique freeze-dried tablet in which drug is physically entrapped or dissolved within the matrix of fast dissolving carrier material. When Zaydis units are put into the mouth, the freeze- dried structure disintegrates instantaneously and does not require water to aid swallowing. The Zaydis matrix is composed of many materials designed to achieve a number of objectives. To impart strength and resilience during handling, polymers such as gelatine, dextran or alginates are incorporated. These form a glossy amorphous structure, which imparts strength. To Obtain Crystallinity, elegance and hardness, saccharides such as mannitol or sorbitol are incorporated. Water is used in the manufacturing process to ensure production of porous units to achieve rapid disintegration while various gums are used to prevent sedimentation of dispersed drug particles in the manufacturing process. Collapse protectants such as glycine prevent the shrinkage of Zaydis units during freeze-drying process or long term- storage. Zaydi'sproducts are packed in blister packs to protect the formulation from moisture in the environment.

Durasolv technology[37-40]

Durnacol is the patented technology of CIMA labs. Durnacol has much higher mechanical strength due to use of the higher compaction pressure during tableting.

Drawback associated with dorsal technology is that the technology is not compatible with larger doses of active ingredients, because the formulation is subjected to high pressure during compaction. This technology is good for tablets having low amount of active ingredients. It consists of drug, filler and a lubricant. Tablets are prepared by using conventional tableting equipment and have good rigidity. These can be packaged into conventional packaging system like blisters.

Orasolv technology[32, 41-45]

CIMA labs have developed Oriol technology. The tablet matrix breaks up within one minute, and the coated drug powder remains left behind. Costing of the drug powder and effervescence are measures of taste masking in Oriol. By this technology, the tablet is produced by the low compression process. It uses an effervescent disintegrant pair that releases gas upon contact with water. Effervescent agents are used in concentrations of 20 – 25% of the total weight of the tablet. Currently,six marketed products are available, which are based on this technology: four Triaminic Soft chew formulations, and each of Tempera First Tabs and Remeron Sol Tab.

Orodis technology[46]

Odoris is compressed technology, have a fast disintegration time (15 to 30 s). This technology produces very hard tablets, which are easy to handle. Tablets can be packed in push- through blisters. Materials used in this technology meet USP and EP standards.

Wow tab technology [32, 47- 49]

The WOW in the WOWTAB signifies the tablet is to be given without water. This technology utilizes sugar and sugar like excipients. The two different types of saccharides arecombined to obtain a tablet formulation with adequate hardness and fast dissolution rate. High moldability saccharides like maltose, mannitol, sorbitol, and oligosaccharides (good binding property) and low moldability like lactose, glucose, mannitol, xylitol (rapid dissolution). The active ingredient is mixed with saccharides and compressed into tablet. Because of the significant hardness the WOWTAB formulation is more stable to the environment than ZYDIS and ORASOLV. WOWTAB technology is patented by Yamanouchi Pharmaceutical Co.

Oraquiick technology[50-53]

KV pharmaceutical claim its micro mask microsphere technology, has superior mouth feel over other taste masking options. The taste masking process does not require any solvent and therefore production is faster and more efficient. Heat sensitive drugs are produced conveniently by or quick technology. Rarick claims quick dissolution in a matter of seconds, with good taste- masking. The tablets can be compressed to achieve remarkable mechanical strength without disrupting.

Nanocrystal technology[54]

Elan's proprietary Nanocrystal technology can enable formulation and improve compound activity and final product properties. On decreasing the particle size, surface area will increase, this leads to an increase in dissolution rate. Pharmacokinetics benefits of orally administered nanoparticles (< 2 microns) in the form of a rapidly disintegrating tablet matrix. Nano crystal colloidal dispersions of drug substance are combined with water soluble GRAS (Generally Regarded asSafe) ingredients, filled intro blisters, and lyophilized. In this method, highly potent drugs and hazardous drugs avoids manufacturing process such as granulation (wet), blending and tableting.

Quick dis technology [33]

Laishram has invented an ideal intra- oral mouth dissolving drug delivery system, which satisfies the unmet needs of the market. It is a thin, flexible, and quick- dissolving film. The film is placed on the top or floor of the tongue. The disintegration time of 2 mm Quick-Dis film is only 5-10 s. The dissolving time which is defined as the time at which not less than 80% of the tested film is dissolved in aqueous media, is around 30 s.

Flashdose technology [45]

Flash dose technology has been patented by fuss. Nurofen melt let, a new form of ibuprofen as melt in mouth tablets prepared using flash dose technology is the first commercial product launched by bio ail corporation. Flash dose tablets consist of self – binding shear from matrix termed as "floss". Shear from matrix is prepared by flash heat processing.

Flashtab technology [33,26]

This technology produces tablets by compression of granular excipients. Combination of Shear form and Deform technologies is used, to mask the bitter taste of the drug. Floss, a sugar-based matrix, which is made up of a mixture of excipients alone or in combination with drugs, is used to form tablets. Nurofen melt let, as a mouth dissolving tablet is prepared by this technology. The product is launched by Bio avail Corporation.

Advatab technology[25,33]

This was developed by Errand Pharmaceuticals.It produces ODT tablets based on a proprietary tablet composition, designed and patented by Kyowa Hakko Kogyo (Tokyo, Japan), in which the lubrication is applied onto each tablet by utilizing a spray during the manufacturing process. Advara is produced by using 10-30 times less hydrophobic lubricant and these tablets can be 30-40 % stronger than the conventional tablets.

Pharmaburst technology[36,45]

Pharmaburst technology is patented by SPI Pharma. Pharmaburst technology uses off the shelf coprocessed

excipients to create an ODT that, depending on the type of active ingredients and loading, dissolves within 30-40 seconds. The process involves a dry blend of a drug, flavour and lubricant that are compressed into tablet on a standard tablet press with stock tooling. The manufacture process can be carried out under normal temperature and humidity conditions.

Frosta technology [33,45]

Highly plastic granules are compressed at low pressure to produce strong tablets with high porosity. The highly plastic granules comprise three types of components: a poriferous and plastic material, a water penetration enhancer, and a binder. Tablets can be made by mixing porous, plastic material with a water penetration enhancer at certain ratios. During granulation, the binder secures the porous material and water penetration enhancer. If the binder is in the liquid or semi-solid state, it should not destroy the porous structure of the porous materials. Aqueous binder solutions with very low water activity.

Excipients commonly used for ODTS preparation[12,26,38]

Mainly seen excipients in FDT are as follows at least one disintegrant, diluent, lubricant, and swelling agent, permeabilizing agent, sweeteners, and flavouring.

Super disintegrants

Crosspovidone, Microcyrstalline cellulose, Sodium starch glycollate, sodium carboxy methyl cellulose, Pregelatinzed starch, Calcium carboxy methyl cellulose and modified corn starch. Sodium starch glycollate hasgood flowability than crosscamellose sodium. Cross povidone is fibrous nature and highly compacctable.

Flavours

Peppermint flavour, cooling flavour oils and flavouring aromatic oil, peppermint oil, clove oil, bay oil, anise oil, eucalyptus oil, thyme oil, oil of bitter almonds. Flavouring agents include, Vanilla, citrus oils, fruit essences.

Sweeteners

Aspartame, Sugars derivatives.

Fillers

Directly compressible spray dried Mannitol, Sorbitol, Xylitol, Calcium carbonate, Magnesium carbonate, Calcium phosphate, Calcium sulphate, Pregelatinized starch, Magnesium trisilicate, aluminium hydroxide.

Lubricants

Stearic acid, Magnesium stearate, Zinc state, Calcium state, talc, polyethylene glycol, liquid paraffin, magnesium lauryl sulphate, colloidal silicone dioxide.

Sugar based excipients

Another approach to fast dissolving tablets by direct compression is the use of sugar- based excipients (e.g., dextrose, fructose, is malt, maltose, mannitol, sorbitol, starch hydrolyse, polydextrose, and xylitol), which display high aqueous solubility and sweetness, and hence, impart taste masking and a pleasing mouthfeel.

Method of disintegrant

Disintegrants are substances or mixture of substances added the drug formulation that facilitates the breakup or disintegration of tablets or capsule content into smaller particles that dissolve more rapidly than in the absence of disintegrants. Superdisintegrants are Croscarmellose, Crosspovidone, Sodium starch glycolate which represent example of a cross linked cellulose, cross linked polymer and a cross linked starch respectively.

The requirement placed on the tablet disintegrant should be clearly defined. The ideal disintegrant has
Poor solubility
Poor gel formation
Good hydration capacity
Good melding and flow properties
No tendency to form complexes with the drugs.
Disintegrants are essentially added to tablet granulation for causing the Compressed tablet to break or disintegrate when placed in aqueous environment.

Methodof superdisintegrants

Internal Addition
External addition

Mechanism[16,39]

Swelling

The most widely accepted general mechanism of action for tablet disintegration is swelling. Tablets with high porosity show poor disintegration due to lack of adequate swelling force.

Porosity and capillary action

Disintegration by capillary action is always the first step. When we put the tablet into suitable aqueous medium, the medium penetrates into the tablet and replaces the air adsorbed on the particles, which weakens the intermolecular bond and breaks the tablet depends upon hydrophilicity of the drug/ excipients an on-tablet conditions. For these types of disintegrants maintenance of porous structure and low interfacial tension towards aqueous fluid is necessary which helps in disintegration by creating a hydrophilic network around the drug particle.

Due to disintegrating particle/particle repulsive forces

Another mechanism of disintegrant attempts to explain the swelling of tablet made with non swellable disintegrants.

Guyot- Hermann has proposed a particle repulsion theory based on the observation that no swelling particle also causes disintegration of tablets. The electric repulsive forces between particles are the mechanism of disintegration and water is required for it. Repulsion is secondary to Wicking.

Due to deformation

During tablet compression, disintegrated particles get deformed and these deformed particles get into their normal structure when they come in contact with aqueousmedia or water. Occasionally, the swelling capacity of starch was improved when granules are extensively deformed during compression. This increase in size of the deformed during compression. This increase in size of the deformed particles produces a breakup of the tablet.

Evaluation of fast dissolving tablets
Organoleptic properties

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

Hardness

A Mechanical 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 tester.

Table 2:ODT products available in international market [12,19]

Nipagin MD	Nimesulide	Prompt cure pharma
Imodium lingual	Imodium	R.P. Scherer Corp., U.S. A
Pepcid inArpita	Pepcid	Merck & C0., U.S.A
ClaritinRedi tabs	Claritin	Schering Plough, U.S. A
Nurofen flash tab	Ibuprofen	Boot healthcare
Hyoscyamine sulfate ODT	Hyoscyamine sulfate	Ethel Corporation
Coaligned Fast	Ibuprofen	Novartis consumer Health
Zyprexa	Olanzapine	Eli Lilly
Zofran ODT	Ondansetron	Glaxo Smith Kline
Risperdal M Tab	Risperidone	Janssen
Imodium Instant Melts	Loperamide HCL	Janssen
Propulsor Quick Sol	Tiapride monohydrate	Janssen
Zooming-ZMT and Raiment	Zolmitriptan	Astra Zeneca
AL avert	Loratadine	Wyeth Consumer Healthcare
NuLev	Hyoscyamine sulfate	Schwarz Pharma
Kepstra	Baclofen	Schwarz Pharma
Benadryl Fast Melt	Diphenhydramine citrate	Pfizer
Nausea OD	Reposition HCL	Yamanouchi
Gaster D	Famotidine	Yamanouchi
Excedrin Quick Tabs	Acetaminophen	Bristol- Myers Squibb
Zolpidem ODT	Zolpidem tartrate	Bio avail
Fluoxetine ODT	Fluoxetine	Bio avail

Friability [44,36]

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

Wetting time and water absorption ratio [58]

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 wettingtime 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 10 cm diameter are placed in a Petridis. Ten millilitres of water-soluble dye solution are added to Petridis. A tabletis 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 Petridis is noted (Wb). The wetted tablet from the Petridis is taken and reweighed (WA). The water absorption ratio, R can be the determined according to the following equation

.

$$R = 100 (WA- Wb) / Wb$$

Moisture uptake studies [43]

Moisture uptake studies for ODT should be conducted to assess the stability of the formulation. Ten tablets from each formulation were kept in a desiccator over calcium chlorideat 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 desiccator 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.

Disintegration test [57]

The time for disintegration of ODTs is generally < 1 min and actual the disintegration time that patients can experience ranges from 5 to 30 s. 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.

Dissolution test [46]

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 it is used less frequently due to specific physical properties of tablets.

Specifically tablet fragments or disintegration tablet masses may become trapped on the inside top of the basket at the spindle where little or no effective stirring occurs, yielding irreproducible results in dissolution profile.

Future prospects

These dosage forms may be suitable for the oral delivery of drugs such as protein and peptide- based therapeutics that have limited bioavailability when administered by conventional tablets. These products usually degrade rapidly in the stomach. Injections generally are not favoured for use by patients unless facilitated by sophisticated auto- injectors. Inhalation is one good alternative system to deliver these drugs, but the increased research into biopharmaceuticals so for has generated predominantly chemical entities with low molecular weights. The developments of enhanced oral protein delivery technology by ODTs which may release these drugs in the oral cavity are very promising for the delivery of high molecular weight protein and peptide.

CONCLUSION

Fast Dissolving Tablets are dosage forms which are formulated to disintegrate or dissolve rapidly in the saliva generally within few seconds. FDTs offer more advantages over conventional dosage forms. Orally disintegrating tablets have better patient compliance and may offer improved biopharmaceutical properties, improved efficacy, and rapid onset of action. ODTs are good alternative for drug delivery to geriatric and Pediatric patients. Even bitter drugs can be incorporated in FDTs by taste masking agents[58]. Nowadays, ODTs are more widely available as OTC products for the treatment of allergies, cold, and flu symptoms. FDTs can be prepared by several methods based on the drug and additives used. Normally ODTs possess less mechanical strength. ODTs can be prepared by some new technologies and additives with sufficient mechanical strength. The main use of development of the fast-dissolving tablet is to maximize its pre structure by vacuum drying and freeze- drying techniques. Subliming agent is added to increase porosity of the tablets in caseof vacuum drying technique. The potential for such dosage forms is promising because of the availability of new technologies combined with patient demand and market acceptance[59]. More advances in technologies, pharmaceutical operations can take advantage of ODTs for product line extension. ODT has tremendous scope for being the delivery system for most of the drugs in future. The emergence of more novel technologies for ODTs in the future days to come with development of new pharmaceutical excipients.

REFERENCES

1. Sastry SV, Stidham JR, Fix JA. Recent technological advances in oral drug delivery: A Review. *Pharmaceutical Science and Technology Today*. 2000; 3: 138-145.
2. Hirani J, Rathod D, Vakala K. Orally disintegrating tablets, *Tropical Journal of Pharmaceutical Research* 2009; 8(2): 161-172.
3. Garg A, Gupta M, Taste Masking and formulation development and evaluation of mouth dissolving tablets of levocetirizine dihydrochloride. *Journal of Drug Delivery and Therapeutics*, 2013; 3(3): 123-130.

4. Sharma D, Chopra R, Bedi N, "Development and Evaluation of Paracetamol Taste Masked Orally Disintegrating Tablets of Perindopril.
5. Fu Y, Yang S, Jeong SH, Kimura S, Park K. Orally fast disintegrating tablets: Developments, technologies, taste masking and clinical studies. *Critical Review in Therapeutic Drug Carrier System*. 2004; 21: 433-76.
6. European Directorate for quality of medicines. Pharmaeuropa. 1998; 10 (4): 547.http://www.pheur.org. Accessed 6 February 2007.
7. Kumaresan C, Orally Disintegrating Tablet- Rapid Disintegration, Sweet Taste, And Target Release Profile, Pharmainfo.net Sep 9 2008.
8. Shaikh S, Chiragra R V, Quazi A. Fast Disintegrating Tablets: An overview of Formulation and Technolgy. *Inter J. Pharmacy pharma science*. 2010; 2 (3): 9-15.
9. Hablb W, Khankari R, Hontz J. Fast dissolving drug delivery system. Critical Reviews in Therapeutic Drug Carrier Systems 2000; 17(1): 61-72.
10. Behnke K. Sogard J. Martin S. Bauml J. Ravindran AV. Agren H, et al. Mirtazapine orally disintegrating tablet versus sertraline; a prospective onset of action study, *Journal of Clinical Psychopharmacology* 2003: 23 (4): 358-364.,
11. Velmurugan S and Sundar Vinushika, Oral Disintegrating Tablets: An Overview, *International Journal of Chemical and Pharmaceutical Sciences* 2010, Dec., Vol 1 (2).
12. Reddy L.H, Ghosh B, and Rajneesh.Fast Dissolving drug delivery systems: a review of the literature. *Indian Pharmaceutical Science* . 2002; 64(4) : 331-336.
13. Camarco W, Ray D and Druffner A: Selecting superdisintegrants for orally disintegrating tablet formulations. Pharmaceutical Technology supplement 2006 \
14. Reddy AM, Babu PS, Harshita B, Sravya R. Conventional and patented technologies in Oral dispersible tablets: a review. *Journal of Chemical and Pharmaceutical Science Review and Research* 2010; 4(2): 87-96.
15. Bhardwaj S, Jain V, Sharma S, Jat RC and Jain S : Orally disintegrating tablets: a review . Drug Invention Today 2010; 2(1) : 81-88.
16. Superdisintegrants: an introduction to chemistry and performance. April 12, Sandipan kundu , P.K. Sahoo recent trend in the development of orally disintegrating tablets *pharmatimes*Apr 2008; 40 (4).
17. Ramjiyani KM, Jethra SI, Patel MR, Fast dissolving tablets: novel approach to drug delivery. World Journal of Pharmaceutical Research 2015: 4 (3) : 1197- 1215.
18. Prateek S, Gupta R, Singh U, Chaturvedi A, Gulati A. Sharma M. Fast dissolving tablets: a new venture in drug delivery. *American Journal pf PharmTechResearch* 2012 : 2 (4): 252-279.
19. Jalmini M, Ranga S, Kumar A. Sharma S, Chauhan BS. A review on immediate release drug delivery system by using design of experiment. *Journal of drug discovery and Therapeutic*2013 : 1 (12) : 21-27.
20. Kapse NK, Bharti VP, Birajdar AS, Munde AV, Panchal PP, Co-processed super disintegrants: novel technique for design orodispersible tablets. *Journal of innovations in Pharmaceutical and biological science* 2015:(4): 541-555.
21. Jeong SH, Takalshi Y, FuY, Park K. Materials properties for making fast dissolving tablets by a compression method, *Journal of Materials Chemistry*2008: 18 (1): 3527-3535.
22. Yourong FU, Shicheng Yang, Seong Hoon Jeong, Susumu Kimura, & Kinam Park; Orally Fast Disintegrating Tablets: Developments, Technologies, Taste – masking and Clinical studies, Critical Reviews in Therapeutic Drug Carrier Systems, 2004, 21 (6) 433-475.
23. Saxena Vaibhav, Khinchi Mahaveer Pr, Gupta MK, Agarwal Dilip and Sharma Natasha. Orally Disintegrating Tablet: Friendly Dosage Form. IJRAP 2010, 1 (2) 399-407.
24. Priyank Patel 1, Sandip Makwanal,Urvish Jobanputral, Mihir Ravatl, Ankit Ajmeral, Mandev. Sublingual route for the systemic delivery of Ondasetron disadvantage from October- December 2011| Vol 76: 309-326.
25. DAali Shukla, Sanjay Singh. Mouth dissolving tablets: An overview of formulation technology Scientia Pharmaceutical Review, 2009 Vol 76: 309-326.
26. Jaysukh J Hirani, Dhaval A Rathod, Kantilla R Vedalia. "Orally Disintegrating Tablets: A Review. "Tropical *Journal of Pharmaceutical Research*, 1 2009; 8(2): 161- 172.
27. Vani R, Rasheed A. Formulation of hydrochlorothiazide and ramipril mouth dissolving tablet using different superdisintegrants. *International Journal of Pharma Science and Research* 2014: 5(1): 207-212.
28. Siden R, Wolf M. Disintegration of chemotherapy tablets for oral administration in patients with swallowing difficulties. *Journal of Oncology Pharmacy Practice* 2013: 19 (2): 145-150.
29. Brown D. Orally Disintegrating tablets. Taste over speed. Drug delivery Tech, 2001: 3(6): 58-61.
30. Lies MC, Atherton AD, Copping NM. Freeze- dried dosage forms and methods for preparing the same. US Patent 5, 188,825 (1993).
31. Sugihara M, Hidaka M, Saitou A. Discriminatory features of dosage form and package. *Jon J Hosp Pharm*, 1996; 12: 322-328.
32. Cirri M, Valleri M, Mura P, Masterly F and Ballerina R. Development of Fast dissolving tablets of flurbiprofencyclodextrin complexes. Drug Development and Industrial Pharmacy. 2005; 31 (7): 697-707.
33. Adel M, Semreen MK and Qato KM, superdisintegrants for solid dispersions to produce Rapidly DisintegratingTenoxicam Tablets*via* Camphor sublimation, Pharmaceutical Technology. 2005; 2: 68.
34. Nautiyal U, Singh S, Singh R, Gopall, Kaka S. Fast dissolving tablets as a novel boon: a review, *Journal of Pharmaceutical, Chemical and biological Sciences*2014: 2 (1): 5-26.

35. Kaur T, Gill B, Kumar S, Gupta GD, Mouth dissolving tablets; A novel approach to drug delivery. *International Journal of Current Pharmaceutical Research* 2011; 3(1): 1-7.
36. Deshmukh KR, Vidyanand P, Shekhar V, Pandey Ak, Dewangan P. A review on mouth dissolving tablet techniques. *International Journal of Research in Ayurveda and Pharmacy 2011*; 3 (1): 1-7.
37. Tayebi H, Mortazavi AS, Formulation and evaluation of a novel Matrix – Type Orally Disintegrating Ibuprofen Tablet. *Iranian Journal of Pharmaceutical Research* 2001: 10 (3): 469-479.
38. Khankari RK, Hintz J, Chastain SJ, Katzner L. Rapidly dissolving robust dosage form. US Patent. 2000.
39. Amborn J, Tiger V, Apparatus for handling and packaging friable tablets. US Patent. 2001.
40. Gohel M, Patel M, AgarwalR andDev R. Formulation Design and Optimization of Mouth Dissolve Tablets of Nimesulide Using Vacuum Drying Technique.AAPS Pharm Sci Tech 3, 2004, 36.
41. Allen LV, Wang B and Davis JD. US Patent. 1998; 5: 807 & 567.
42. Nandy BC, Mazumder B, Pathak elk, Saxena N, Jain S, Sharma S, et al. An overview on fast dissolving drug delivery system. Asian *Journal of Pharmaceutical Sciences and Research* 2012; 1 (2): 1-30.
43. Khirwadkar P, Dashora K. A review: fast dissolving drug delivery system: Current developments in novel system design and technology. *International Journal of Biomedical and Advance research* 2012; 3(2): 82-100.
44. Wehling F, Schedule S, Madamala N.Effervescent dosageform with microparticles. US Patent. 1993
45. Wehling F, Schedule S, Base coated acid particles andeffervescent formulation incorporating same. US Patent. 1996.
46. Ghosh T, Ghosh A, Prasad D. A review on new generation orodispersible tablets and its future prospective. *International Journal of Pharmacy and Pharmaceutical Sciences* 2010; 3 (1): 1-7.
47. Acosta C, Tabare R and Ouali A. US Patent.1998; 5: 807.
48. Mizumoto T, MaudaY, Fukul M. Intra buccally dissolving compressed moldings and production process thereof. US Patent 1996.
49. Mizumoto T, Masuda Y, Kajiyama A. Yanagisawa M, Nyshadham JR.Tablets quicklydisintegrating in the oral cavity and process for producing the same. US patent. 2003.
50. Sharma D, Kumar D, Singh M, Singh G, Rathore MS. Fast disintegrating tablets: a new era in novel drug delivery system and new market opportunities. *Journal of Drug Delivery and Therapeutics* 2012: 2 (3): 74-86.
51. Prabhakar V, Agarwal S, Chauhan R, Sharma S. Fast Dissolving tablets: an overview, *International Journal of Pharmacy and Pharmaceutical Sciences Review and Research*
52. Fatma R, Nandi PK, Gupta AK. Novel approach for patient's compliance; fast dissolving tablets. *World Journal of Pharmacy and Pharmaceutical Sciences* 2014; 3 (7): 1758-1768.
53. Prajapati BG, Ratnakar N, Review onrecent patents on fast dissolving drug delivery system. *International journal of Pharm Tech Research*2009: 1 (3): 790-798.
54. Kaushik D, Dureja Hand Saini TR.Orally disintegrating tablets: An Overview of melt- in mouth tablet technologies and techniques, Tablets, Capsules, 2004: 2: 30-36.
55. Roshan K, Bharkatiya M, Rathore KS, Kumar SS, Sirvi G, Somani N. Fat Dissolving tablet drug delivery system an overview. *International Journal of Pharmacy* 2015; 1 (5): 250-256.
56. Panigrahi D, Baghel S and Mishra B, Mouth dissolving tablets: An overview of preparation techniques, Evaluation and patented technologies*. J. Pharma Research* 2005; 4 (3): 33-41.
57. Shailesh Sharma. New generation of tablet: Fast dissolving tablet. Pharmainfo.net. 2008; 6 (1): 111-119.
58. Ravichandiran V, Masilamani V, Kumar SS, Kumaragurubaran T, Senthilnathan B, Kamalakkannan V. Fast Dissolving Tablets: A Review, *Journal of Pharmacy Research*. 2011; 4(8): 2590-2592
59. Sharma N, Sharma J, Jat RC, Rathore AS, Fast is dissolving tablets as novel dosage form, *International Journal of Research and development in Pharmacy and Life Sciences.*2012; 1(3): 90-104.
60. Erande, K., Joshi, B., Mouth Dissolving Tablet: A Comprehensive Review, 2013; 2 (7): 26-28.
61. Shaikh S., Khirsagar, R.V., Quazi, A Fast-Disintegrating Tablets an overview of formulations and technologies, *Int. J of Pharmacyand Pharma Sci,* 2010; 2 (3): 9-11