



“FORMULATION AND EVALUATION OF FAST DISINTEGRATING TABLET OF ATORVASTATIN CALCIUM”

Mr. Manish Kumar Chaudhary, Mr. Kashif Hussain, Dr. Yogita Tyagi, Mr. Praveen Kumar Ashok

Gyani Inder Singh Institute of Professional Studies, Dehradun, Uttarakhand

Designation & Address of Corresponding Author: Manish Kumar Chaudhary

Gyani Inder Singh Institute of professional studies, Dehradun, Uttarakhan.

Master in pharmacy (Quality Assurance)

ABSTRACT:

Fast dissolving tablets have developed as one of the most popular and generally recognized dose forms, particularly for young patients with inadequate muscle and neurological system development, as well as for seniors suffering from Parkinson's disease or hand tremors. Few solid dosage forms, such as capsules and tablets, are currently experiencing difficulties such as difficulty swallowing (dysphagia), leading to high rates of noncompliance and rendering the therapy ineffective. For many drugs, the oral dosage form and route of administration are the most recommended methods of administration; nonetheless, they have limitations such as first-pass metabolism, psychiatric patients, immobile patients, and uncooperative patients. FDTs dissolve or disintegrate quickly in saliva without the need for water. Fast dissolving tablets dissolve quickly in saliva.

Keywords: Fast dissolving tablets, FDTs, Superdisintegrants, Mouth dissolving tablets, MDTs

INTRODUCTION:

The US Food and Drug Administration (USFDA) defines a fast dissolving tablet (FDT) as "a solid dosage form containing a medicinal substance or active ingredient that disintegrates rapidly, usually within seconds, when placed on the tongue."

Oral medicine delivery is very common. The tablet is the most frequent dosage form available today. It has the advantages of ease of administration, compactness, simple production, and possible cost savings. Many people have difficulty swallowing pills and hard gelatin capsules and do not take medication as prescribed. Honda and Nakano

conducted a survey. Half of the patients reported difficulty swallowing medications such as tablets and capsules, resulting in a high rate of noncompliance and ineffective therapy. The problem is most acute in pediatric and geriatric patients, but it also affects adults who are sick in bed and active working patients who are busy or traveling, particularly those with diabetes.

According to recent market research, FDTs are favored over other dose forms by more than half of the patient population. The majority of mouth dissolving tablets are made using one of two methods. The first is the use of super disintegrants such as crospovidone, sodium starch glycolate, and croscarmellose sodium. Another method is to freeze and vacuum dry the tablets to increase the pore structure. Because of its ease of use, quick procedure, and low cost, direct compression is common in all approaches.

Some medications' bioavailability may be improved as a result of drug absorption in the oral cavity, as well as pregastric absorption of pharmaceuticals in saliva that flow down into the stomach. Furthermore, the amount of medication susceptible to first pass metabolism is reduced when compared to regular tablets.

Requirements of fast disintegrating tablets:

Patient factors:

Fast dissolving dosage forms are appropriate for individuals who are unable to swallow regular tablets and capsules, notably juvenile and geriatric patients. These include the following:

- Patients who have difficulty in swallowing or chewing solid dosage forms.
- Patients in compliance due to fear of choking.
- Very elderly patients of depression who may not be able to swallow the solid dosage forms
- An eight-year-old patient with allergies desires a more convenient dosage form than antihistamine syrup.
- A middle-aged patient undergoing radiation therapy for breast cancer may be too nauseous to swallow her H2-blocker.
- A schizophrenic patient who may try to hide a conventional tablet under his or her tongue to avoid their daily dose of an atypical antipsychotic.
- A patient with persistent nausea, who may be a journey, or has little or no access to water.

Effectiveness factors:

These formulations make a big deal about increased bioavailability and faster onset of action. In circumstances where the medicine dissolves fast, dispersion in saliva in the oral cavity induces pre-gastric absorption of some formulation ions. Many drugs are absorbed through the buccal, pharyngeal, and gastric regions. Any pre-gastric absorption avoids first pass metabolism and can be a significant advantage in medications that undergo hepatic metabolism. Furthermore, safety profiles for drugs that produce significant amounts of toxic metabolites via first-pass liver metabolism and gastric metabolism, as well as drugs with a significant fraction of absorption in the oral cavity and pre-gastric segments of GIT, may be improved.

Manufacturing and marketing factors:

As a drug's patent expiration date approaches, it is common for pharmaceutical companies to develop a given drug entity in a new and improved dosage form. A new dosage form allows a firm to gain market exclusivity, differentiate their product, and extend patent protection. For example, in response to a generic challenge filed in the United States by Ranbaxy, Eisai Inc. developed Aricept FDT, a line extension of donepezil for Alzheimer's disease, in Japan in 2004 and in the United States in 2005.

Advantages of fast dissolving tablets:

- No need of water to swallow the tablet.
- FDTs can be easily administered to pediatric, elderly and mentally disabled patients.
- Accurate dosing as compared to liquids.
- Dissolution and absorption of the drug is fast, offering rapid onset of action.
- Bioavailability of drugs is increased as some drugs are absorbed from mouth, pharynx and esophagus through saliva passing down into the stomach.
- Advantageous over liquid medication in terms of administration as well as transportation.
- First pass metabolism is reduced, thus offering improved bioavailability and thus reduced dose and side effects.
- Offering improved safety.
- Suitable for sustained/controlled release actives.

Limitations of FDTs:

- The major disadvantages of FDTs is related to the mechanical strength of tablets.
- FDT are very porous and soft molded metrics or compressed in a tablet with low compression, which makes tablet friable and brittle which difficult to handle.
- Bad tastes drugs are difficult to formulate as FDT; special precaution should have to be taken before formulate such kind of drug.
- Several FDT are hygroscopic cannot maintain physical integrity under normal condition from humidity which requires specialized package.
- Dryness of the mouth due to decreased saliva production may not be good candidates for these tablet formulations.
- Rate of absorption from the saliva solution and overall bioavailability.
- Drug and dosage form stability.

Challenges to develop FDTs**Palatability**

Because most drugs are unpleasant to swallow, FDTs usually contain the medication in a flavor-masked form. FDTs breakdown or dissolve in the patient's oral cavity, releasing active chemicals that come into contact with the taste buds. As a result, disguising the taste of the medications becomes crucial to patient compliance.

Mechanical strength and disintegration time

To allow FDTs to disintegrate in the oral cavity, they are either made of a very porous and soft-molded matrix or compressed into tablets with very low compression force, which makes the tablets friable and/or brittle, difficult to handle, and frequently necessitating specialized peel-off blister packing, which may increase the cost. Only the wow tab and durasolv technologies can create tablets that are hard and durable enough to be packaged in multi-dose bottles.

Hygroscopicity

Several orally disintegrating dosage forms are hygroscopic and cannot maintain physical integrity under normal temperature and humidity conditions. As a result, they require humidity protection, necessitating the use of specialist product packaging.

Amount of drug

The amount of medicine that can be included into each unit dose limits the utilization of FDT technologies. For lyophilized dosage forms, the drug dose must be less than 400 mg for insoluble medications and 60 mg for soluble pharmaceuticals. This parameter is especially difficult to formulate when creating fast-dissolving oral films.

Aqueous solubility

Water-soluble medications present a variety of formulation issues because they produce eutectic mixtures, resulting in freezing-point depression and the creation of a glassy solid that may collapse upon drying due to loss of supporting structure during the sublimation process. Such collapse can occasionally be avoided by employing matrix-forming excipients such as mannitol, which can promote crystallinity and hence contribute stiffness to the amorphous composite.

Size of tablet

The size of a pill influences its ease of administration. The easiest size of tablet to swallow is 7-8 mm, whereas the easiest size to handle is one larger than 8 mm. As a result, it is challenging to obtain a tablet size that is both portable and easy to manage.

Mouth feel

In the oral cavity, FDTs should not break into larger particles. The particles formed following FDT disintegration should be as tiny as possible. Furthermore, the addition of flavors and cooling agents such as menthol improves the mouth feel.

Sensitivity to environmental conditions

FDTs should be resistant to environmental conditions such as humidity and temperature because the majority of the materials used in FDTs are designed to dissolve in a small amount of water.

Techniques for preparing fast dissolving tablets:**Conventional technologies****Various conventional manufacturing techniques for FDDDS****Freeze-drying or lyophilization**

It is a pharmaceutical procedure that permits the drying of heat sensitive pharmaceuticals and biologicals at low temperatures using a vacuum to remove water by sublimation. Drugs are dissolved or dispersed in an aqueous solution of a carrier, transferred to prefabricated blister packs, treated to a nitrogen flush to freeze out, and then stored in the refrigerator to complete the procedure. Lyophilization processes have great porosity and specific surface area, and they dissolve quickly in the mouth, resulting in high medication bio-availability. The main disadvantage of this method is its high cost, time-consuming procedure, and fragility, which makes traditional packing inappropriate for packing this dosage form and causes stability concerns under stress conditions.

Advantages

The main benefit of utilizing this process is that the tablets produced have a very short disintegration time and a superb tongue feel due to the fast melting effect.

Moulding Method

Tablets are made with hydrophilic components to achieve optimum medication dissolution. The powder mass is soaked in a hydro alcoholic solvent before being compacted into a dosage form. After then, the solvent system is allowed to evaporate. Spray congealing a molten combination of hydrogenated cottonseed oil, sodium carbonate, lecithin, polyethene glycol, and an active component into lactose-based tablet triturate produces the taste of medication particles. The moulding procedure is particularly porous since solvents are eliminated by drying, producing a porous aggregate that favors quick disintegration.

Melt Granulation

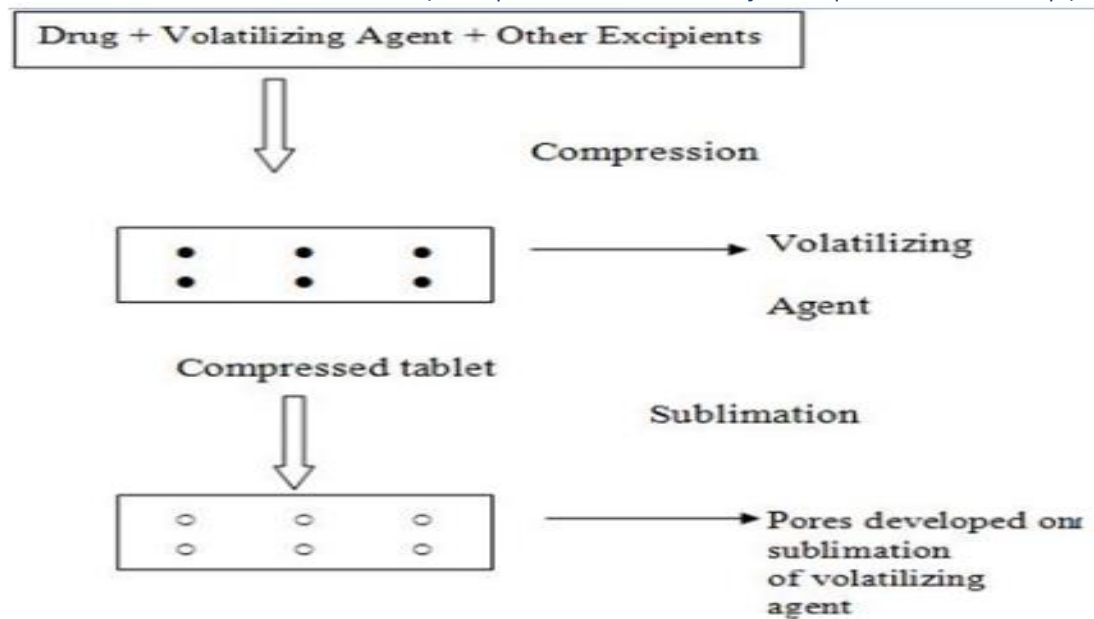
The melt granulation technique is a method of agglomerating medicinal powders using a meltable binder. The advantage of this approach over traditional granulation is that neither water nor organic solvents are required. Because there is no drying step, the process takes less time and uses less energy than wet granulation. It is a technique for increasing the dissolution rate of medications that are weakly water soluble, such as griseofulvin.

Mass-extrusion

Using methanol as a solvent and polyethene glycol, which is water soluble, to soften the mixture of components, it is then extruded into thin cylinders which are then further cut into small tablets using a heated blade. With this technique, bitter-tasting medications can be covered up by creating small granules that increase oral bioavailability.

Sublimation

By combining inert solid substances that volatilize quickly, such as urea, camphor ammonium carbonate, ammonium bicarbonate, and hexamethylene-tetramine, into porous mass, one can achieve rapid disintegration and dissolution. They were compressed after being combined with additional components. By reducing pressure and raising the temperature just a bit, the volatile material is released, leaving the mass in a porous state. They are porous in nature and may be treated with solvents like cyclohexane and benzene, which are sublimation process



characteristics.

Direct compression

The disintegrant addition technology (direct compression) is the method most frequently used to create tablets because it has the following benefits:

- High doses can be accommodated and final weight of the tablet can exceed that of other methods.
- The easiest way to manufacture the tablets.
- Conventional equipment and commonly available excipients are used.
- A limited no. of processing steps are involved.
- Cost effectiveness.

Patented technologies for fast dissolving tablets

The fast dissolving property of FDTs is often attributed to the tablet matrix's rapid breakdown as a result of the rapid penetration of water. A number of pharmaceutical businesses have developed and patented technologies based on formulation-related elements and diverse processes. Patented technology is defined as follows:

Zydis Technology

The drug is physically entrapped or dissolved inside a matrix of quickly evaporating carrier material in the one-of-a-kind Zydis formulation freeze-dried tablet. When Zydis units are put in the mouth, the freeze-dried structure rapidly dissolves and does not need water to make swallowing easier. A range of components designed to achieve a variety of objectives make up the Zydis matrix. Gelatin, dextran, and alginates are a few examples of polymers that are utilized to increase strength and resilience during handling. These come together to create a glossy, amorphous structure that strengthens.

Limitations

- The amount of drug could be incorporated should generally be less than 400 mg for insoluble drugs and less than 60 mg for soluble drugs.

- The particle size of the insoluble drugs should not be less than 50 μm and not more than 200 μm to prevent sedimentation during processing.

Advantages

- Buccal pharyngeal and gastric regions are all areas of absorption from this formulation. Any pre-gastric absorption avoids first-pass metabolism and can be an advantage in drugs that undergo a great deal of hepatic metabolism.
- The Zydis formulation self-preserving because the final water concentration in the freeze-dried product is too low to allow for microbial growth.
- Patients who have difficulty swallowing oral medication due to dysphagia, stroke or medical conditions such as gastro esophageal reflux disease, multiple sclerosis or Parkinson's disease.

Disadvantages

- The process of freeze-drying is a relatively expensive manufacturing process.
- The formulation is very lightweight and fragile, and therefore should not be stored in backpacks or the bottom of purses.
- It has poor stability at higher temperatures and humidities.
- A water insoluble drug can be incorporated only up to 400 mg per tablet or less. On the other hand water, the soluble drug can be incorporated only up to 60 mg.

Orasolv Technology

CIMA labs is the company that created the Orasolv technology. The active medication is taste-masked in this system. The effervescent disintegrating agent is also present. To reduce the amount of time needed for oral dissolving, tablets are manufactured using the direct compression technique at low compression force. The tablets are produced using standard blenders and tablet presses. The manufactured tablets are packaged in specialized pick and place systems and are soft and friable.

Advantages

There are two types of taste-masking: rapid absorption. One milligram to 750 milligram medication strengths have been produced using this method. The disintegration period of the tablet can be planned in the range of 10 to 40 seconds, depending on formulation and tablet size.

Disadvantages

Due to the presence of the effervescent system, they are sensitive to moisture and need to be stored properly. Low strength mechanically.

Durasolv Technology

The unique technique of CIMA labs is called Durasolv. This method creates tablets with a medication, fillers, and lubrication. Typical tableting equipment is used to create tablets, which have a fair degree of stiffness. These can be contained in standard packaging systems, such as blisters. A technique like Durasolv is suitable for goods that only need small amounts of active chemicals.

Advantages

The Durasolv technology produces a more durable ODT when tablets are crushed to a harder 15-100 N hardness and contain low amounts of active substances (125 mcg to 500 mg). As a result, this technique allows for flexible packaging; tablets can be packaged in bottles and blisters.

Disadvantages

Larger doses of active substances cannot be used with this approach since they would be compressed under high pressure. Durasolv's medication powder covering could fracture during compaction, exposing the patient's taste buds to the bitter pharmaceuticals.

Wow Tab Technology

Wow, Yamanouchi Pharmaceutical Co. has patented the tab technology. "Without Water" is the acronym WOW. To create a quickly melting, robust tablet, a combination of low mold ability and high mold ability saccharides is used in this technique. To create tablets with an appropriate hardness, high and low mold ability are combined.

Advantages

Adequate rate of dissolution and hardness. Wow, the packaging options for tab products include both blister packs and traditional bottles.

Disadvantages

No significant change in bioavailability.

Dispersible Tablet Technology

Patents were granted to Lek in Yugoslavia for dihydroergotamine and cimetidine dispersible pills, which were advertised as dissolving in water at room temperature in less than a minute. Water does not readily dissolve dihydroergotamine in its free basic form. Dispersible tablets containing 0.8-10%, preferably about 4% by weight, of organic acids led to an enhanced dissolving rate of dihydroergotamine methanesulphonate. A disintegrating agent is one of the crucial excipients in the formulation of cimetidine. It allows for speedy swelling and/or wetting of the pills, which causes them to dissolve quickly. Starch or modified starches, microcrystalline cellulose, alginic acid, cross-linked sodium carboxymethylcellulose, and cyclodextrin polymers are some of the disintegrating agents. Better disintegration results were obtained when two or more disintegrating agents were used.

CONCLUSION

Fast dissolving tablets are novel dosage forms that were created and specifically created to address some of the issues with conventional solid dosage forms, such as the difficulty in swallowing the pill in elderly and young patients. Fast-dissolving pills are made to dissolve or disintegrate in the saliva in a matter of seconds, usually between 5 and 60. When compared to traditional oral dosage forms, fast-dissolving tablets have better patient compliance and acceptance. They may also have better biopharmaceutical properties, bioavailability, improved efficacy, convenience, and safety.

Over the past ten years, FDTs have become incredibly more popular. For patients who are psychotic, bedridden, elderly, or young, for those who might not have access to water, or for patients who are actively traveling, FDTs

must be developed. FDT formulations created using some of these traditional and patented technologies are sufficiently strong mechanically and quickly dissolve in the mouth without the use of water. The more recent technologies used in the development of FDTs that provide more advantageous dosage forms with fewer drawbacks

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