

THE PHARMA INNOVATION

Fast Dissolving Drug Delivery and its Technologies

Samita Gauri^{1*}, Gaurav Kumar

1. P.D.M College of Pharmacy, Bahadurgarh, Haryana, India

It is very well known that a drug can be administered through many different routes so as to produce a systemic pharmacological effect. The route of administration is considered as the path by which a drug is taken into the body for the treatment of various diseases and disorders. The main route of administering a drug administration is the oral route which is the oldest and most commonly used because of its ease of administration, self-medication and avoidance of pain as compared to parental route. Despite of the tremendous advancement in oral route some of the people find difficulty in swallowing tablet and other oral dosage form, so in order to troubleshoot all these problem associated with oral route, fast dissolving drug delivery systems (FDDS) were first came into existence in 1970 as an alternative to tablets, syrups and capsules, for pediatric and geriatric patients which rapidly disintegrate and dissolve in saliva and then easily swallowed without need of water which is a major benefit over conventional dosage form.

Keyword: Oral route, Fast dissolving drug delivery system, Pediatric and Geriatric

INTRODUCTION: Despite of so much of advancements in various delivery system developed for administration of various drugs through different routes such as oral, parental, transdermal and nasal etc., the oral route is considered as the preferred route of administration which includes painless, ease of administration, patient friendly and so on^{1,2}. Several new technologies had been developed for oral delivery is being available to address to improve the patient compliance³. Fast dissolving drug delivery system (FDDS) is gaining popularity in pharmaceutical companies as they are new drug delivery technique in order to provide the patient with medicine without

obstacles in swallowing⁴. FDDS include tablets and films. Fast dissolving tablets are designed in such a way that they disintegrate and then swallowed without the need of water as compared to other conventional dosage form⁵. Films are the small polymeric strips which when placed on the mucosal surface rapidly dissolve within a fraction of seconds in order to release the active ingredients without the consumption of water^{6,7}.

IDEAL CHARACTERISTICS OF FAST DISSOLVING DRUG DELIVERY SYSTEM^{7,8}

- Require no water for administration
- Cost effective production methods
- Leave minimal or no residue in mouth
- Dissolve within a fraction of seconds
- Have a pleasant mouth feel

Corresponding Author's Contact information:

Samita Gauri*

P.D.M. College of Pharmacy, Bahadurgarh, Haryana, India

E-mail: rohilla3@gmail.com

ADVANTAGES OF FDDS⁸

- Ease of administration
- Water consumption is not required
- Rapid dissolution and absorption of drug
- Bioavailability is increased

FAST DISSOLVING TABLETS

Orally disintegrating dosage forms has to be placed in mouth and then get dispersed in saliva without the need of water. Orally disintegrating tablets are also called as oral disperse, mouth dissolving, rapidly disintegrating, fast melt, and quick dissolve system⁹.

PATENTED TECHNOLOGIES FOR FAST DISSOLVING TABLETS AND FAST DISSOLVING FILMS

New FDDS technologies are addressing many pharmaceutical companies to enhance the life cycle management to convenient dosing for geriatrics and paediatrics⁸. Various technologies of fast dissolving tablets are:

1. DURASOLV TECHNOLOGY

DuraSolvR technology was developed by Ciba to provide stronger tablets for packaging in blisters or bottles. The key ingredients in this formulation are filler and lubricant. The particle size of the filler is preferably between about 20 and 65 μm . Fillers, such as dextrose, mannitol, sorbitol, lactose, and sucrose, have the advantage of quick dissolution and avoid some of the grittiness. The tablets have low friability, which is about 2%. The disintegration time is less than 60 seconds. The lubricant blending times can also be increased to 10–25 minutes or longer. This method can produce tablets by using the direct compression method, conventional tableting methodologies and conventional package equipment. Thus, the production cost is significantly reduced¹⁰.

2. ZYDIS TECHNOLOGY

It is the first marketed new tablet technology. In this the drug is produced by freeze drying or lyophilizing the drug in gelatin matrix. The product thus

produced is very light weight and packed in blister packs. It also utilizes microencapsulation using specialized polymers and resins hence mask the bitter taste of drug. This technology claims for increased bioavailability as compared to other conventional tablets. The main advantage of this technology is convenience and disadvantage is that the freeze drying process is quite expensive manufacturing process. Zydis formulation should be used within six month from opening¹¹.

3. OROSOLV TECHNOLOGY

This technology is being patented by CIMA Labs. This includes the use of effervescent disintegrating agents which is compressed with low pressure to produce the fast dissolving tablets. The evolution of carbon dioxide from the tablet produces a fizzing sensation, which is a positive organoleptic property. The concentration of effervescent mixture usually employed is 20-25% of tablet weight¹².

4. FLASH DOSE TECHNOLOGY

The FlashDose technology uses a unique spinning mechanism so as to produce a floss-like crystalline structure, much like cotton candy. This crystalline sugar can then incorporate the drug and be compressed into a tablet. This procedure had been patented by Fuisz and is known as Shear form. The final product which is being produced has a very high surface area for dissolution. It disperses and dissolves quickly once placed on the tongue. The Flash dose tablets consist of self-binding shear form matrix termed as “floss”¹³.

5. FLASH TAB TECHNOLOGY

The Flashtab technology is yet another fast dissolving/disintegrating tablet formulation.

Prographarm laboratories have patented the Flashtab technology. It utilizes most

of the same excipients as in conventional compressed tablets. A disintegrating agent and a swelling agent are used in combination with coated drug particles in this formulation to produce a tablet that disintegrates in the mouth in less than one minute¹⁴.

6. WOW TAB TECHNOLOGY

WOWTAB technology employs a combination of low- and high-moldability saccharides in order to produce fast-dissolving tablets using conventional granulation and tableting techniques. The typical low-moldability saccharides include lactose, mannitol, glucose, sucrose, and xylitol and high-moldability saccharides are maltose, sorbitol, and oligosaccharides. When tablets are made by compressing a saccharide having low and high moldability alone, the desired properties of adequate hardness and quick disintegration in the mouth cannot be achieved simultaneously. Moreover, if saccharides having low moldability and high moldability are mixed (physical mixture) before tableting, quick disintegration and dissolution in the mouth cannot be obtained. For this reason, a saccharide having low moldability was granulated with a saccharide having high moldability as a binder¹⁵.

7. QUICKSOLV TECHNOLOGY

Quicksolv (Janssen Pharmaceutica, Beese, Belgium). In the Quicksolv formulation, the matrix compositions are dissolved in the solvent (usually water), and then this solution is frozen. At the temperature the first solvent will remain in the solid form, and then the frozen solution contacts the second solvent which is usually, ethanol, menthol, or acetone. Thus, the first solvent is removed after a few hours of contacting the second solvent to result in a usable matrix. The final product

disintegrates almost instantly. This method is claimed to prevent or to reduce the incidence of cracking during the final preparation, having uniform porosity and also the adequate strength for handling¹⁵.

8. LYCO

Lyoc utilizes a freeze drying process but it differs from Zydis in that the product is frozen on the freeze dryer shelves. In order to prevent homogeneity by sedimentation during this process, these formulations also require a large proportion of undissolved inert filler such as mannitol, to increase the viscosity of the in process suspension. The high proportion of filler used reduces the potential porosity of the dried dosage form and hence results in denser tablets with disintegration rates that are comparable with the loosely compressed fast melt formulations¹².

9. PHARMABRUST TECHNOLOGY

Pharmaburst technology is being patented by SPI pharma. The tablet manufactured by this process involves a dry blend of a drug, flavors, and lubricant then followed by compression into tablets which then dissolve within 30-40 seconds. Tablets manufactured by this methodology have sufficient strength can be packed in blister packs and bottles¹⁶.

FAST DISSOLVING FILMS

It is a new type of formulation in FDDDS that provides a very convenient means of taking medications. In this technique, a solution is prepared containing water soluble film forming polymer (pullulan, hydroxypropyl methylcellulose, carboxy methylcellulose, hydroxyl ethylcellulose, hydroxyl propylcellulose, polyvinyl pyrrolidone, polyvinyl alcohol or sodium alginate, etc.), drug and other taste masking ingredients, which was then allowed to form a film after evaporation of solvent. This film, when placed in mouth, melts

or dissolves rapidly, releasing the active drug in mouth. The film is stamp size thin films of size less than 2X2 inches, it dissolve rapidly in mouth within a fraction of seconds¹⁸.

TABLE 1: MARKETED PREPARATION OF ORODISPERSIBLE TABLETS¹⁷

Trade name	Active drug	Manufacturer
Ugesic	Piroxicam	Mayer organic Ltd.
Torrox MT	Rofecoxib	Torrent pharma
Esulide MD	Nimesulide	Doff Biotech
Vomidon md	Domperidon	Olcare lab
kazoldil MD	Nimesulide	kaizen drugs
Zofer MD	Ondansetron	Sun pharma
Mosid md	Mosapride	Torrent pharma
Valus	Valdecocixib	Galen mark .
Ondem MD	ondencetrom	Alkem pharma
Nimulid MDT	Nimesulide	Panacea Biotech
Rofixx md	Rofecoxib	Cipla ltd. Mumbai ,India
Olanex Istab	Olanzapine	Ranbaxy Labs Ltd
Romilast	Montelukast	Ranbaxy Labs Ltd
Zontec MD	Cetirizine	Zosta pharma India
Nime MD	Nimesulide	Maiden pharma
Lonazep MD	Olnazepine	Sun pharma

TECHNOLOGIES FOR FAST DISSOLVING FILMS:

1. SOLULEAVES

In this technology the film is produced in order to release the active ingredients on coming in contact with saliva. This method is especially useful for pediatric and geriatric patients who may have difficulty swallowing conventional tablets. SOLULEAVES are designed in

such a way that they adhere to mucous membrane in order to release the drug slowly in 15mins¹⁹.

2. FOAMBURST

FOAMBURST is a new patent granted in September 2004 which is for capsules made of foamed film. Gas is blown into the film during production, resulting in a film with a honeycombed structure. The voids in the film may be gas-filled, empty or filled with other materials to produce specific taste-burst characteristics or to deliver active drugs. The light honeycombed structure results in capsules that dissolve rapidly, causing a melt-in-the-mouth sensation¹⁹.

3. XGEL

XGel film Technology developed by BioProgress was causing a revolution in the product offerings and manufacturing methods, which was now available to the pharmaceutical industry. XGel film, potentially enhance the product stability. The films may be coloured or printed during manufacture for branding and coding which is a useful mechanism to enhance product identification and has also been developed for non-ingestible applications such as cosmetic, ostomy pouches, sanitary and healthcare devices^{20,21}.

4. WAFERTAB

WaferTab is a unique, innovative, and highly stable edible film dose form. WaferTab is a drug delivery system which incorporates pharmaceutical actives into an ingestible film strip. It provides rapid dissolution and release of active pharmaceutical ingredient when the strip comes into contact with saliva in the mouth. The WaferTab film strip can also be flavoured for additionally improved taste-masking. The active ingredient is integrated into the body of a fused. The film can be prepared in a variety of shapes and sizes and is an ideal method for delivering medicines which require fast

release and also for use by patients who have difficulty swallowing²².

TABLE 2: MARKETED PREPARATION OF ORAL FILMS²³

Manufacturer	Product	Drug or supplement
NOVARTIS	Theraflu Thin Strip Long Acting Cough	Dextromethorphan
NOVARTIS	Theraflu Thin Strip Multi-Symptom	Diphenhydramine
NOVARTIS	Thaminic Thin Strip Long Acting Cough	Dextromethorphan
NOVARTIS	Triaminic Thin Strip Cough and Runny Nose	Diphenhydramine
NOVARTIS	Gas-X Thin Strip Anti Gas	Simethicone
Prestige Brands	Little Colds Sore Throat Strips	Pectin
InnoZen	Suppress Cough Strips	Dextromethorphan
InnoZen	Suppress Herbal Cough Relief Strips	Menthol
Prestige Brands	Chloaseptic Relief Strips	Benzocaine: Menthol

CONCLUSION

The FDTs have potential advantages over conventional oral dosage forms with their improved patient compliance; convenience, bioavailability and rapid onset of action which drawn the attention of many manufactures over a decade. FDT formulations obtained by some of these technologies have sufficient mechanical strength, quick disintegration/dissolution in the

mouth. Many drugs can be incorporated in FDT especially unpalatable drugs. The research is still going on. More products need to be commercialized to use this technology properly. Thus FDT may be developed for most of the available drugs in near future. Fast disintegrating tablets have better patient compliance and may offer improved biopharmaceutical properties, improved efficacy and better safety compared with conventional oral dosage forms. Today, fast disintegrating tablets are more widely available as over-the-counter products for the treatment of allergies, cold and flu symptoms. The target population has expanded to those who want convenient dosing anywhere, anytime, without water. The future potential for these products is promising because of the availability of new technologies combined with strong market acceptance and patient demand. Future possibilities for improvements in Rapid disintegrating and drug delivery are bright, but the technology is still relatively new. Several drug delivery technologies that can be leveraged on improving drug therapy from these dosage forms. The application of OTFs now extends beyond traditional immediate release oral dosage forms. Development of topical films, probiotic strips, and controlled-release OTF products are new forms made possible through this delivery format's flexibility, proven robustness and stability. The future of OTF formulation and processing is a direct reflection of evolving healthcare needs. Demographically, most established markets have aging populations that benefit from simple, easy-to-dispense and dose products. As emerging markets require flexibility in the number of units dispensed at any given time and providers continue to look for options that can increase compliance, minimize dosage levels and frequency, and reduce costs. OTFs have increasingly become the solution to satisfy all of these needs. In addition development teams are able to capitalize on the flexibility of OTFs by adapting the technology for their program.

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