ISSN: 2279 - 0594

Journal of Biomedical and Pharmaceutical Research 2 (1) 2013, 08-18

REVIEW ARTICLE

A Review on Fast Dissolving Tablet Technology.

***Lalji Amipara, M.M.Gupta**

Jaipur college of pharmacy, Jaipur(Rajasthan), India.

ABSTRACT

Fast dissolving Tablets are disintegrating and/or dissolve rapidly in the saliva without the need for water. Some tablets are designed to dissolve in saliva remarkably fast, within a few seconds, and are true fast-dissolving tablets. Others contain agents to enhance the rate of tablet disintegration in the oral cavity, and are more appropriately termed fast-disintegrating tablets, as they may take up to a minute to completely disintegrate. Oral delivery is currently the gold standard in the pharmaceutical industry where it is regarded as the safest, most convenient and most economical method of drug delivery having the highest patient compliance. This tablet format is designed to allow administration of an oral solid dose form in the absence of water or fluid intake. Such tablets readily dissolve or disintegrate in the saliva generally within <60 seconds. Fast- or mouth dissolving tablets have been formulated for pediatric, geriatric, and bedridden patients and for active patients who are busy and traveling and may not have access to water. Such formulations provide an opportunity for product line extension in the Many elderly persons will have difficulties in taking conventional oral dosage forms (viz., solutions, suspensions, tablets, and capsules) because of hand tremors and dysphagia. Swallowing problems also are common in young individuals because of their underdeveloped muscular and nervous systems. Other groups that may experience problems using conventional oral dosage forms include the mentally ill, the developmentally disabled, and patients who are uncooperative, on reduced liquid-intake plans, or are nauseated. In some cases such as motion sickness, sudden episodes of allergic attack or coughing, and an unavailability of water, swallowing conventional tablets may be difficult.

INTRODUCTION

Recent trends in Pharmaceutical formulation development technology have presented viable dosage alternatives for patients who may have difficulty swallowing tablets or liquids. Traditional tablets and capsules administered with an 8-oz. (One glass) of water may be inconvenient or impractical for some patients. However, some patients, particularly pediatric and geriatric patients, have difficulty swallowing or chewing solid dosage forms. Many pediatric and geriatric patients are unwilling to take these solid preparations due to fear of choking. For example, a very elderly patient may not be able to swallow a daily dose of antidepressant in the form of a Caplet shaped Tablet. An eight-year-old with allergies could use a more convenient dosage form than antihistamine syrup. A schizophrenic patient in the institutional setting can hide a conventional tablet under his or her tongue to avoid their daily dose of an atypical antipsychotic. A middle-aged woman undergoing radiation therapy for breast cancer may be too nauseous to swallow her H2-blocker. Fast-dissolving tablets (FDTs) / Orally disintegrating tablets (ODTs) are a perfect fit for all of these patients. Fast-dissolving drug delivery systems have rapidly gained acceptance as an important new way of administering drugs. There are multiple fast-dissolving OTC and Rx products on the market worldwide, most of which have been launched in the past 3 to 4 years. There have also been significant increases in the number of new chemical entities under development using a fast-dissolving drug delivery technology.

SALIENT FEATURES OF FAST DISSOLVING DRUG DELIVERY SYSTEM:

1. Ease of administration for patients who are mentally ill, disabled and uncooperative.
2. Requires no water.
3. Quick disintegration and dissolution of the dosage form.
4. Overcomes unacceptable taste of the drugs.
5. Can be designed to leave minimal or no residue in the mouth after administration and also to provide a pleasant mouth feel.
6. Allows high drug loading.
7. Ability to provide advantages of liquid medication in the form of solid preparation. Adaptable and amenable to existing processing and packaging machinery.
8. Cost-effective.

SIGNIFICANCE OF ORAL DISINTIGRATING TABLET:

Oral Disintegrating Tablets offer dual advantages of solid dosage forms and liquid dosage forms along with special features which include:

ACCURATE DOSING:

Being unit solid dosage forms, provide luxury of accurate dosing, easy Portability and manufacturing, good physical and chemical stability and an ideal alternative for pediatric and geriatric patients.

ENHANCED BIOAVAILABILITY:

* ***Corresponding author:*** Lalji Amipara, ***/ Email:*** lvamipara88@gmail.com,

Bioavailability of drugs is enhanced due to absorption from mouth, pharynx and esophagus.

RAPID ACTION:

Fast onset of therapeutic action as tablet gets disintegrated rapidly along with quick dissolution and absorption in oral cavity.

PATIENT COMPLIANCE:

No need of water to swallow the dosage form. Hence, it is convenient for patients who are traveling and do not have immediate access to water.

EASE OF ADMINISTRATION:

Convenient to administer specially for geriatric, pediatric, mentally disabled and bed ridden patients who have difficulty in swallowing.

OBSTRUCTION FREE:

No risk of suffocation in airways due to physical obstruction when swallowed, thus providing improved safety and compliance.

ENHANCED PALATABILITY:

Good mouths feel, especially for pediatric patients as taste masking technique is used to avoid the bitter taste of drug.

SIMPLE PACKAGING:

No specific packaging required. It can be packaged in push through blisters.

BUSINESS AVENUE:

Provide new business opportunities in the form of product differentiation, line extension, uniqueness and life cycle management.

COST EFFECTIVE:

Conventional processing and packaging equipments allow the manufacturing of tablets at low cost.

CHARACTERISTICS OF FAST DISSOLVING DELIVERY SYSTEM:

1. Ease of administration: Fast Dissolving Delivery Systems are easy to administer and handle hence, leads to better patient compliance. Usually, elderly people experience difficulty in swallowing the conventional dosage forms (tablets, capsules, solutions and suspensions) because of tremors of extremities and dysphasia.

2. Taste of the medicament: As most drugs are unpalatable, mouth dissolving delivery systems usually contain the medicament in taste masked form. Delivery systems dissolve or disintegrate in patient's mouth, thus releasing the active ingredients which come in contact with the taste buds and hence, taste masking of the drugs becomes critical to patient compliance.

3. Hygroscopicity: Several fast dissolving dosage forms are hygroscopic and cannot maintain physical integrity under normal condition from humidity which calls for specialized product packaging.

4. Friability: In order to allow fast dissolving tablets to dissolve in the mouth, 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 which are difficult to handle, often requiring specialized peel-off blister packaging.

5. Mouth feel: Mouth feel is critical, and patients should receive a product that feels pleasant. Any large particles from the disintegrating tablet that are insoluble or slowly soluble in saliva would lead to an unpleasant gritty feeling. This can be overcome by keeping the majority of the particles below the detectable size limit. In some cases, certain flavors can imbibe an improved mouth feel perception, resulting in a product that is perceived as being less gritty, even if the only change is the flavor. Effervescence can be added to aid disintegration and improve mouth feel by reducing the "dryness" of a product.

CONVENTIONAL TECHNIQUES USED IN THE PREPARATION OF FAST DISSOLVING DRUG DELIVERY SYSTEM:

Various technologies used in the manufacture of Fast dissolving tablets include:

- Freeze drying or lyophilization
- Tablet Molding
- Direct compression
- Spray drying
- Sublimation
  Taste masking
- Mass extrusion
- Cotton Candy process
- Melt Granulation
- Phase Transition
- Nanonization
  Fast Dissolving Films

1. FREEZE-DRYING OR LYOPHILIZATION:

Freeze drying is the process in which water is sublimed from the product after it is frozen. This technique creates an amorphous porous structure that can dissolve rapidly. Commonly used excipients with their uses and examples employed in manufacturing of fast dissolving tablets using Freeze-drying are listed on next page. A typical procedure involved in the manufacturing of fast dissolving tablets using this technique is mentioned here. The active drug is dissolved or dispersed in an aqueous solution of a carrier/polymer. The mixture is dosed by weight and poured in 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 aluminum foil backing is applied on a blister-sealing machine. Finally the blisters are packaged and shipped

The freeze-drying technique has demonstrated improved absorption and increase in bioavailability. The Zydis formulations consist of a drug physically trapped in a water-soluble matrix (saccharine mixture and polymer), which is freeze dried to produce a product that dissolves rapidly when placed in mouth. The ideal candidate for Zydis technology should be chemically stable and water insoluble and particle size preferably less than 50 micron. Water soluble drugs might form eutectic mixtures and not freeze adequately, so dose is limited to 60 mg and the maximum drug limit is 400 mg for water insoluble drug as large particle sizes might present sedimentation problems during manufacture.

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

2. TABLET MOULDING:

The preparation of fast dissolving tablets 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. Molding process is of two types i.e. solvent method and heat method. Solvent method involves moistening the powder blend with a hydro alcoholic solvent followed by compression at low pressures in molded plates to form a wetted mass (compression molding). The solvent is then removed by air-drying. The tablets manufactured in this manner are less compact than compressed tablets and possess a porous structure that hastens dissolution.

The heat molding process involves preparation of a suspension that contains a drug, agar and sugar (e.g. Mannitol or lactose) and pouring the suspension in the blister packaging wells, solidifying the agar at the room temperature to form a jelly and drying at 30˚C under vacuum. The mechanical strength of molded tablets is a matter of great concern. Binding agents, which increase the mechanical strength of the tablets, need to be incorporated. Taste masking is an added problem to this technology.

3. 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 fast dissolving tablets. 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 croscarmellose sodium 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.

4. SUBLIMATION:

The key to rapid disintegration of fast dissolving tablets 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 pthalic 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.

5. DIRECT COMPRESSION:

There was no much attention to the direct compression of pharmaceuticals in the previous days (late 1950s). Now a days great deal of attention has been given to both product and process development. The availability of new materials, new forms of old materials and the invention of new machinery has allowed the production of tablets by simplified and reliable methods. In early 1960's, the introduction of spray dried lactose (1960) and avicel (1964) had changed the tablet manufacturing process and opened avenues of direct compression tableting.

Previously, the word direct compression was used to identify the compression of a single crystalline compound (i.e. sodium chloride, potassium chloride, potassium bromide, etc.) into a compact form without the addition of other substances. Current usage of the term direct compression is used to define the process by which tablets are compressed directly from the powder blends of active ingredient/s and suitable excipients. No pre-treatment of the powder blends by wet or dry granulation is involved.

Direct compression represents the simplest and most cost effective tablet manufacturing technique. This technique can now be applied to preparation of fast dissolving tablets because of the availability of improved excipients especially superdisintegrants and sugar based excipients. Direct compression, using directly compressible excipients is the most commonly used method of preparing fast dissolving tablets. Directly compressible excipients are very coarse and granular in nature and give a coarse dispersion in the mouth with decreased mouth feel and compliance. It is very difficult to prepare fast dissolving tablets with drugs having very low bulk density, higher dose and poor flow property using this technique.

6. DRY GRANULATION TECHNIQUE:

The fast dissolving tablets has been prepared by means of dry granulation technology, which has the following advantages over other techniques of preparation:

1. It can be used for all types of drugs including moisture sensitive and heat sensitive.

2. It can be used for drugs having very low bulk density

3. It can be used for poorly compressible drugs and drugs having poor flow property.

4. The tablets can be packed into regular bottles, blister, strip pack or sachets.

5. The tablets can be stored in bulk in drums to be packaged subsequently. Moreover conventional tablet packaging feeders can be used for packing purpose. The process of dry granulation is cost effective as it avoids solvents, and the processes of drying like freeze drying, spray drying etc.

6. This reduces overall reduction in capital expenditure (conventional processing, packaging, and storage facilities). These dosage forms may be in the form of tablets, wafers, granules, or granules packed as such along with other pharmaceutically acceptable additives in a suitable package which upon contact with water, saliva or aqueous solution disintegrates within a few seconds.

7. COTTON CANDY PROCESS:

The cotton candy process is also known as the "candy floss" process and forms the basis of the technologies such as Flash Dose (Fuisz Technology). A fast dissolving tablets is formed using a candyfloss or shear form matrix; the matrix is formed from saccharides or polysaccharides processed into amorphous floss by a simultaneous action of flash melting and centrifugal force. The matrix is then cured or partially recrystallised to provide a compound with good flow properties and compressibility. The candyfloss can then be milled and blended with active ingredients and other excipients and subsequently compressed into fast dissolving tablets. However the high processing temperature limits the use of this technology to thermo stable compounds only.

8. MASS EXTRUSION[5]:

This technology involves softening the active blend using the solvent mixture of water-soluble polyethylene glycol and methanol and subsequent 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 for bitter drugs and thereby achieve taste masking.

NEW ORALLY DISINTEGRATING DOSAGE FORMS:

ORAL FILMS AND WAFERS:

Oral films and wafers are the newer technologies in the manufacturing of orally disintegrating dosage forms. They are thin elegant films of edible water-soluble polymers of various sizes and shapes like square, rectangle or disc. The strips may be flexible or brittle, opaque or transparent. They are designed to provide rapid disintegration on the tongue without the need for water. They have the advantage of a large specific surface area for disintegration. One or a combination of the following processes like hot-melt extrusion; solid dispersion extrusion, rolling and solvent casting are used to manufacture these films. A major limitation of these dosage forms is low drug loading capacity and limited taste masking option.

PHASE TRANSITION

Kuno et al proposed a novel method to prepare ODTs with sufficient hardness by involving the phase transition of sugar alcohol. In this technique, ODTs are produced by compressing and subsequently heating tablets that contain two sugar alcohols, one with high and other with a low melting point. Heating process enhances the bonding among particles leading to sufficient hardness of tablets which was otherwise lacking owing to low/little compatibility.

MELT GRANULATION:

Melt granulation is a process in which pharmaceutical powders are efficiently agglomerated by the use of binder which can be a molten liquid, a solid or a solid that melts during the process. For accomplishing this process, high shear mixers are utilized, where the product temperature is raised above the melting point of binder by a heating jacket or by the heat of friction generated by

impeller blades. Perissutti et al prepared carbamazepine fast-release tablets by melt granulation technique using polyethylene glycol 4000 as a melting binder and lactose monohydrate as hydrophilic filler.

NANONIZATION:

A recently developed Nanomelt technology involves reduction in the particle size of drug to nano size by wet-milling technique. Surface adsorption of the nano crystals of the drug is done on selected stabilizers for stabilizing them against agglomeration, which are then incorporated into MDTs. This technique is mainly advantageous for poor water soluble drugs and also for a wide range of doses (up to 200 mg of drug per unit).

FAST DISSOLVING FILMS:

It is a newer developing front in MDDDS that provides a very convenient means of taking medications and supplements. In this technique, water soluble film forming polymer (pullulan, CMC, HPMC, HEC, HPC, PVP, PVA etc.), drug and other taste masking ingredients are dissolved in non-aqueous solvent to prepare non-aqueous solution, which on evaporation of solvent forms a film. Resin adsorbate or coated micro particles of the drug can be incorporated into the film if the drug is bitter. This film when placed in mouth, melts or dissolves rapidly and release the drug in solution or suspension form. This system forms the thin films of size less than 2 X 2 inches which dissolves within 5 sec with instant drug delivery and flavored taste.

Each technology has a different mechanism, and each fast-dissolving / disintegrating dosage form varies regarding the following:

* Mechanical strength of final product;
* Drug and dosage form stability;
* Mouth feel;
* Taste;
* Rate of dissolution of drug formulation in saliva;
* Swallow ability;
* Rate of absorption from the saliva solution;
* Overall bioavailability.

POTENTIAL CANDIDATES FOR FAST DISSOLVING TABLETS (FDT):

Several factors must be considered while selecting an appropriate drug candidate for development of orally disintegrating dosage forms. The ultimate characteristics of a drug for dissolution in the mouth and pregastric absorption from ODTs include:

- Free from bitter taste.
- Dose lowers than 20 mg.
- Small to moderate molecular weight.
- Good solubility in water and saliva.
- Partially nonionized at the oral cavity's pH.
- Ability to diffuse and partition into the epithelium of the upper GIT (log P >1, or preferably >2).
- Ability to permeate oral mucosal tissue.

In contrast, the following characteristics may render a drug unsuitable for delivery as an orally disintegrating dosage form:

- Short half-life and frequent dosing.
- Very bitter or unacceptable taste because taste masking cannot be successfully achieved.
- Require controlled or sustained release.
- Combination with anticholinergics.

OTHER EXCIPIENTS USED IN FAST DISSOLVING TABLETS:

Excipients balance the properties of the actives in fast-melting tablets. This demands a thorough understanding of the chemistry of these excipients to prevent interaction with the actives. Determining the cost of these ingredients is another issue that needs to be addressed by formulators. The role of excipients is important in the formulation of fast-dissolving tablets. These inactive food-grade ingredients, when incorporated in the formulation, impart the desired organoleptic properties and product efficacy. Excipients are general and can be used for a broad range of actives, except some actives that require masking agents.

BULKING MATERIALS:

Bulking materials are significant in the formulation of fast-dissolving tablets. The material contributes functions of a diluents, filler and cost reducer. Bulking agents improve the textural characteristics that in turn enhance the disintegration in the mouth, besides adding bulk also reduces the concentration of the active in the composition. The recommended bulking agents for this delivery system should be more sugar-based such as mannitol, polydextrose, lactitol, DCL (direct compressible lactose) and starch hydrolystate for higher aqueous solubility and good sensory perception. Mannitol in particular has high aqueous solubility and good sensory perception. Bulking agents are added in the range of 10 percent to about 90 percent by weight of the final composition.

The excipients could be ranked in descending order in terms of their brittleness:

Microcrystalline cellulose > spray-dried lactose > beta lactose > alpha lactose > alpha lactose monohydrate > dicalcium phosphate dihydrate.

The sugar based excipients which are commonly used are especially bulking agents (like dextrose, fructose, lactilol, maltilol, maltose, mannitol, sorbitol,starch hydrolysate, polydextrose and xylitol) which display high aqueous solubility and sweetness, and hence impart taste masking property and provide pleasing mouth feel.

Mizumitoet al classified sugar-based excipients into two types on the basis of molding and dissolution rate:
Type 1 saccharides (lactose and mannitol) exhibit low mouldability but high dissolution rate.
Type 2 saccharides (maltose and maltilol) exhibit high mouldability but low dissolution rate.

Table 1. Properties of Modified Starches/Celluloses Used in ODTs

Sr. No.	Superdisintegrant	Properties
1	Croscarmellose sodium	High swelling capacity, effective at low concentration (0.5-2.0%), can be used up to 5%.
2	Crospovidone	Completely insoluble in water. Rapidly disperses and swells in water, but does not gel even after prolonged exposure. Greatest rate of swelling compared to other disintegrants. Greater surface area to volume ratio than other disintegrants. Effective concentration (1-3%). Available in micronized grades if needed for improving state of dispersion in the powder blend.
3	Sodium starch glycolate	Absorbs water rapidly, resulting in swelling up to 6%. High concentration causes gelling and loss of disintegration

EMULSIFYING AGENTS:

Emulsifying agents are important excipients for formulating fast-melting tablets they aid in rapid disintegration and drug release without chewing, swallowing or drinking water. In addition, incorporating emulsifying agents is useful in stabilizing the immiscible blends and enhancing bioavailability. A wide range of emulsifiers is recommended for fast-dissolving tablet formulation, including alkyl sulfates, propylene glycol esters, lecithin, sucrose esters and others. These agents can be incorporated in the range of 0.05 percent to about 15 percent by weight of the final composition.

LUBRICANTS:

Lubricants, though not essential excipients, can further assist in making these tablets more palatable after they disintegrate in the mouth. Lubricants remove grittiness and assist in the drug transport mechanism from the mouth down into the stomach.

FLAVOURS AND SWEETENERS:

Flavours and taste-masking agents make the products more palatable and pleasing for patients. The addition of these ingredients assists in overcoming bitterness and undesirable tastes of some active ingredients. Both natural and synthetic flavours can be used to improve the organoleptic characteristic of fast-melting tablets. Formulators can choose from a wide range of sweeteners including sugar, dextrose and fructose, as well as non-nutritive sweeteners such as aspartame, sodium saccharin, sugar alcohols and sucralose. The addition of sweeteners contributes a pleasant taste as well as bulk to the composition.

SUPERDISINTEGRANTS:

Disintegrants are substances routinely included in tablet formulations and in some hard shell capsule formulations to promote moisture penetration and dispersion of the matrix of dosage form in dissolution fluids. An oral solid dosage form should ideally disperse into the primary particles from which it was prepared. Superdisintegrants are generally used at a low concentration, typically 1-10% by weight relative to total weight of dosage unit. Generally employed superdisintegrants are crosscarmellose sodium (Ac-Di-Sol), Crosspovidone (CP), sodium starch glycolate (SSG) etc. which represent example of crosslinked cellulose, crosslinked polymer and crosslinked starch respectively. Selection of appropriate formulation excipients and manufacturing technology is necessary for obtaining the optimized design features of orally disintegrating dosage forms. Ideally, superdisintegrants should cause the tablet to disrupt, not only into the granules from which it was compressed but also into powder particles from which the granules were prepared.

SELECTION OF SUPERDISINTEGRANTS:

Although superdisintegrants primarily affect the rate of disintegration, but when used at high levels they can also affect mouth feel, tablet hardness and friability.

Hence, various ideal factors to be considered while selecting an appropriate superdisintegrants for a particular formulation should:

• Produce rapid disintegration, when tablet comes in contact with saliva in the mouth/oral cavity.
• Be compactable enough to produce less friable tablets.
• Produce good mouth feel to the patients. Thus, small particle size is preferred to achieve patient compliance.
• Have good flow, since it improves the flow characteristics of total blend.

MECHANISM OF ACTION OF DISINTEGRANT:

Various mechanisms proposed in this concern include water wicking, swelling, deformation recovery, repulsion and heat of wetting. It seems likely that no single mechanism can explain the complex behavior of the disintegrants. However, each of these proposed mechanisms provides some understanding of different aspects of disintegrant action.

Table 2. Application of Various Commercially Used Combinations of Modified Cellulose/Starch Used in ODTs

Superdisintegrant and Disintegrants			Applications			
Brand Name	**Common Name**	**Classification**	**Functional Category**	**Properties**	**EMC at 25ºC/ 90%RH**	**Typical Uses**
CL-Kollidon	Crospovidone	Polyvinyl-pyrrolidone	Tablet super Disintegrant	Swelling (18% in 10s), (45% in 20s)	62%	Disintegrant (Dry and Wet granulation)
Ac-DiSol	Croscarmellose Sodium	Cellulose, carboxy-methyl ether, sodium salt crosslinked	Tablet and capsule disintegrant	Wicking and swelling (12% in 10s), (23% in 20s)	88%	Disintegrant for capsules, tablets and granules
Explotab Primojel	Sodium starch glycolate	Sodium carboxymethyl starch	Tablet and capsule super disintegrant	Swelling capacity (300 times)	------	Disintegrant (Dry and Wet granulation)
Explotab V17	Sodium starch glycolate	(Cross linked substituted Carboxy-methyl ether) sodium carboxymethyl starch	Super Disintegrant	More swelling than Explotab		Disintegration & dissolution aid. Not for use in wet granulation
Explotab CLV	Sodium starch glycolate	(Cross linked low substituted Carboxy-methyl ether) Sodium carboxymethyl starch	Super disintegrant	Swelling		Use in wet granulation and high shear equipment
L-HPC	Hydroxypropyl cellulose(low substituted)	Cellulose, 2-hydroxypropyl ether	Tablet and capsule super disintegrant	Swelling (13% in 10s), (50% in 20s)	37%	Disintegrant and Binder in wet granulation
Starch 1500	Starch, Pre-gelatinized	Pregelatinized starch	Diluent , binder and disintegrant	Hygroscopic	22%	Binder/diluent & disintegrant
Avicel	Microcrystalline cellulose	Cellulose	Tablet & capsule diluent, Tablet Disintegrant	Hygroscopic, swelling- (12% in 10s), (18% in 20s)	18%	Binder/diluent, lubricant and disintegrant

TASTE MASKING TECHNOLOGIES:

Taste masking is an essential requirement for fast dissolving tablets for commercial success. Taste masking of the active ingredients can be achieved by various techniques. Drugs with unacceptable bitter taste can be microencapsulated into pH sensitive acrylic polymers. Cefuroxime axetil is microencapsulated in various types of acrylic polymers (e.g., Eudragit E, Eudragit L-55 and Eudragit RL) by solvent evaporation and solvent extraction techniques. These polymer microspheres showed efficient taste masking and complete dissolution in a short period. Fine granules of drug and disintegrant (e.g. low substituted Hydroxypropyl cellulose) when coated with a water insoluble polymer (e.g. ethylcellulose) masked the bitter taste of sparfloxacin. The addition of low substituted Hydroxypropyl cellulose as disintegrant to the drug in cores resulted in increased dissolution rate and bioavailability of sparfloxacin compared to its conventional tablets. Ozer and Hincal reported a simple coacervation method using gelatin, and anhydrous sodium sulphate as coacervating agent for taste making of beclamide. Beclamide is an anti-epileptic drug with unpleasant taste. It is microencapsulated into gelatin, with sodium sulphate as coacervating agent, and glutaraldehyde as hardening agent. The microcapsules after formation are dehydrated using alcohol. The core: wall substance ratio was 1:1, and the taste could be successfully masked. A novel technique for taste masking of macrolides (e.g. erythromycin and clarithromycin) is reported by Yajima . Monoglycerides having a low melting point which can form good elaborate film, and easily soluble in intestine, and polymers which are insoluble in the mouth (pH 5-8), but are freely soluble in stomach (pH 1-4), are selected for taste masking of drugs with unpleasant taste. The polymer is dissolved or dispersed in monoglyceride, and the drug is granulated with above mixture and the resultant granules are cooled.

TRADITIONAL TASTE MASKING TECHNIQUES IN ORAL PHARMACEUTICALS:

Taste masking using flavours and sweeteners: Artificial sweeteners and flavours are generally being used along with other taste-masking techniques to improve the efficiency of these techniques in dentifrices, mouthwashes and cough drops. The examples are given in Table no. 1.

Taste masking using Lipophilic Vehicles: - It is the property of oils, surfactants, polyalcohols and lipids to increase the viscosity in the mouth and to coat the taste buds and therefore they are potential taste masking agents. Formulations with a large excess of lecithin or lecithin like substances are claimed to control bitter taste in pharmaceuticals. Examples are given in Table no. 2.

Taste masking by Coating with Hydrophilic Vehicles: - Carbohydrates can be used as a coating material to mask the taste of orally administered drugs. Various forms of proteins have been used extensively for taste masking. Some examples are given in Table no. 3

Taste masking by Ion-Exchange Resins (IERs):- To stabilize the sensitive components, to sustain the drug release, to disintegrate tablets, and to mask taste, ion-exchange resins are used in formulations. Some examples of drugs and taste masking agents and ion exchange resins are given in Table no.4.

Table 3: Taste masking using flavours and sweeteners

Sr. No.	Drug(s)	Taste masking agent(s)
1.	Aspirin	Sodium phenolate
2.	Chlorpheniramine, Phenyl propanolamine	Sod. bicarbonate, citric acid, orange/cream flavour
3.	Famotidine	Sod. bicarbonate, citric acid, lemon flavour
4.	Ibuprofen	Sod. citrate dihydrate, sod. saccharin, refined sugar
5.	Theophylline	D-sorbitol, sodium saccharin, sodium glutamate, and vanilla essence
6.	Acetaminophen	Sod. bicarbonate, citric acid, cherry flavour
7.	Caffeine	Starch, lactose, and mannitol

Table. 4: Taste masking using lipophilic vehicles

S. No.	Drug(s)	Taste masking agent(s)
1.	Isoprothiolane	Hydrogenated oil and HPMC
2.	Acetaminophen	Molten stearyl stearate
3.	Talampicillin HCl	Magnesium aluminum silicate & soyabean lecithin
4.	Clarithromycin	Glyceryl monostearate and AMCE
5.	Indeloxazine HC	Hydrogenated oil and surfactants

HPMC=Hydroxypropyl methyl cellulose; AMCE=Aminoalkyl methacrylate copolymer E

Table 5. Taste masking using polymer coating

Sr. No.	Drug(s)	Polymer(s) used
1	Pinaverium bromide	Cellulose or shellac
2	Ibuprofen	Methacrylic acid copolymer (Eudragit)
3	Amoxycillin trihydrate	MCC, L-HPC
4	Clarithromycin	Carbopol, PVP
5	Roxithromycin	PEG, Eudragit L 100–55
6	Cefuroxime axetil	Eudragit L-55 and RL
7	Pirenzepine & Oxybutynin	Eudragit E-100, MCC, HPC
8	Levofloxacin	Eudragit E100, cellulose acetate

HPMC= Hydroxypropyl methyl cellulose; HEC= Hydroxyethyl cellulose; HPC=Hydroxypropyl cellulose; L-HPC= Low substituted hydroxypropyl cellulose; CMC= Carboxy methyl cellulose; PVP= Polyvinyl pyrollidone; EC=Ethyl cellulose; MCC= Microcrystalline cellulose; PEG= Polyethylene glycol; Tio2=Titanium dioxide.

Table. 6: List of drugs and taste masking ion exchange resins

S. No	Drug(s)	Resin/complexing agent
1	Carbetapentane citrate	Cyclodextrin
2	Ibuprofen	Hydroxypropyl b-cyclodextrin
3	Diphenhydramine HCl	Indion CRP 244, indion CRP 254
4	Buflomedil	Amberlite IRP 69
5	Orbifloxacin	Amberlite IRP 69

EVALUATION OF BLEND:

The prepared blend was evaluated by following tests.

- Angle of repose
- Bulk density
- Tapped density
- Carr's index
- Hauser's ratio

ANGLE OF REPOSE:

Angle of repose was determined by using funnel method. The accurately weighed blend was taken in a funnel. The height of the funnel was adjusted in such a way that the tip of the funnel just touches the apex of the heap of blend. The drug (as solid dispersion)-excipients blend was allowed to flow through the funnel Freely on to the surface. The diameter of the powder cone was measured and angle of repose was calculated using the following equation: **Tan q = h/r**

Where h and r are the height and radius of the powder conc.

BULK DENSITY:

Apparent bulk density was determined by pouring a weighed quantity of blend into graduated cylinder and measuring the volume and weight.

BD =WEIGHT OF THE POWDER / VOLUME OF THE PACKING:

TAPPED DENSITY:

It was determined by placing a graduated cylinder, containing a known mass of drug-excipients blend. The cylinder was allowed to fall under its own weight onto a hard surface from the height of 10cm at 2- second intervals. The tapping was continued until no further change in volume was noted.

TBD =Weight of the powder / volume of the tapped packing.

COMPRESSIBILITY INDEX:

The Compressibility Index of the blends was determined by Carr's compressibility index.

A similar index has been defined by Hausner ---Hauser's ratio = Tapped density/ Poured density

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

Hausner's ratio >1.25 – Poor flow = 33% Carr

Commercially available fast dissolving tablets in India

Trade Name	Active Drug	Manufacturer
Cefadur DT	Cefadroxil	Cipla (protec)
Cefinar DT	Cefixime	Zydus Alidac
Zofran ODT; Vomokind MD	Ondansetron	Glaxo Wellcome; Mankind

CONCLUSION:

The innovations in the arena of formulating Fast Dissolving Tablets are aimed at both increasing the performance of the dosage form by decreasing the disintegration time and increasing the patient compliance by masking the objectionable taste of the active ingredients. FDT need to be formulated for pediatric, geriatric, bedridden, psychotic patients, for those patients who are busy in traveling, has difficulty in swallowing and may not have access to water. FDT offers the combined advantages of ease of dosing and convenience of dosing in the absence of water or fluid. These achievements require constant up gradation of formulation variables as well as technologies involved in the production of dosage forms. In this article, I have attempted to unveil the strategies that have been used by inventors for improving the performance and acceptability of Fast Dissolving Tablets. The use of superdisintegrants for achieving these aims is not new. However, with the improvement design of new techniques, it has become possible to develop FDTs with reduced content of superdisintegrants and with better mouth feel.

The use of techniques like freeze drying, direct compression and effervescence are highly suitable for formulating stable and acceptable dosage forms of vitamins, enzymes and thermolabile drugs. Which are indeed highly acceptable means of delivery drugs to especially, pediatric and geriatric patients. The development of Durasolv and Orasolv technologies are worth mentioning in this regard. Similarly, considerable research towards producing modified microcrystalline cellulose or starch in order to engineer them suitable for direct compression has significantly reduced the product development time for optimizing FDT formulation.

The application of nanotechnology to formulation is expected to further enhance the acceptance and performance of these dosage forms. However, not much work seems to have been done in this particular specialized area. Nevertheless, judicious use of excipients and technology can be expected to make the task of formulating an acceptable and effective FDT easier than before. However, substantial amount of research remains to be conducted for the development of natural polymer based system which is highly site specific. Furthermore, development of such system correlating well with all desired characteristics for effective delivery would nevertheless be an appropriate futuristic endeavor. Therefore in coming era, there is going to be continued interest for the development of natural polymers based orally disintegrating tablets. The future trends in innovations of drug delivery systems will continue to bring together different technological disciplines and formulation aspects to create novel technologies.

REFERENCES:

1. Sharma S. Pharmainfo.net, 2008; 6(5). Available at: http://www.pharmainfo.net/reviews/ orodispersable-tablet-review.
2. Fu Y, Yang S, Jeong SH, Kimura S, Park K. Crit Rev Ther Drug Carrier Sys. 2004; 21, 433-475.
3. Rakesh Pahwa, Mona Piplani, Prabodh C.Sharma, Dhirender Kaushik and Sanju Nanda; Orally Disintegrating Tablets – Friendly to Pediatrics and Geriatrics; Available online at www.scholarsresearchlibrary.com.
4. CIMA Labs, Inc. CIMA--Technologies. 2 FEB 2011; Available at: http://www.cimalabs.com/tech.htm.
5. Yamanouchi Pharma Technologies, Inc. WOWTAB. 25 JAN 2011; Available at: http://www.ypharma. Com/wowtab .h tml.
6. KV Pharmaceutical Company. Drug Delivery Technologies (technical bulletin); KV Pharmaceutical Company. OraQuick, 2 FEB 2010; Available at: http://www.kvpharma.com/tech/3_1_oraquick.html
7. www. ElanNanoCrystal_Technology.html.
8. Augsburger LL, Brzeczko AW, Shah U. Encyclopedia of Pharmaceutical Technology. 2nd edition.2002; 3, 2623-2638.
9. Kamal Saroha, Pooja Mathur, Surender Verma, Navneet Syan and Ajay Kumar on Mouth dissolving tablets: An Overview on future compaction in oral formulation technologies , Der Pharmacia Sinica, 2010, 1 (1): 179-187; Available at: at www. Pelagiare search library.com.
10. Saxena V et al IJRAP 2010 1(2),399-407; Orally Disintegrating Tablets-A friendly dosage form.
11. Honey Goel, Parshuram Rai et al on Orally Disintegrating Systems: Innovations in Formulation and Technology at Recent Patents on Drug Delivery & Formulation 2008, 2, 258-274.
12. Rajeshree Panigrahi, Saiprasanna Behera on A Review On Fast Dissolving Tablets; URL: http: //www.webmedcentral.com/article_view/809.
13. Shailendra Kumar Singh et al on Fast Disintegrating Combination Tablets Of Omeprazole And Domperidone; Asian Journal of Pharmaceutical and Clinical Research , Vol.2 Issue 3, July-September 2009.
14. Mukesh P. Ratnaparkhi et al; Fast Dissolving Tablet at JPR Vol 2, No 1 (2009): January.

15. D Bhowmik et al; Fast Dissolving Tablet: An Overview at Journal of Chemical and Pharmaceutical Research, 2009, 1(1): 163-177.

16. Prashant Khemariya et al; Preparation and evaluation of mouth dissolving tablets of meloxicam; International Journal of Drug Delivery 2 (2010) 76-80; available online at http:// www . arjournals. org/ ijdd.html.

17. Bhupendra G Prajapati et al; A Review on Recent patents on Fast Dissolving Drug Delivery System; International Journal of PharmTech Research (IJPRIF) Vol.1, No.3, pp 790-798 , July-Sept 2009.