A REVIEW: FAST DISSOLVING DRUG DELIVERY SYSTEM: CURRENT DEVELOPMENTS IN NOVEL SYSTEM DESIGN AND TECHNOLOGY

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Abstract
The oral route of drug administration is the most important method for administering drugs for systemic effects. The oral drug delivery market, in particular, remains the largest segment of the overall drug delivery market, presently valued at $49 billion, and growing at a rate of 10% each year. Except in certain cases the parenteral route is not routinely used for self administration, e.g. insulin. The topical route of administration has only recently been employed to deliver drugs to the body for systemic effects. Therefore fast dissolving drug delivery has received ever-increasing demand during last decade, and the field has become a rapidly growing area in the pharmaceutical industry. Upon introduction into the mouth, these tablets dissolve or disintegrate in the saliva without need of water with good mouth feel property. The popularity and usefulness of the formulation resulted in development of several FDT technologies. 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. This review explains the recent advances in fast dissolving drug delivery systems with special focus on its new breakthrough in various formulation aspects resulted in development of several FDT technologies.

Keywords: FDT technologies, Superdisintegrants, Three dimensional Printing (3DP), Cotton candy process, Ac-Di-Sol, Flashtab technology, Orasolv

1. Introduction:
Recent advances in Novel Drug Delivery System (NDDS) aims to enhance safety and efficacy of drug molecule by formulating a convenient dosage form for administration and to achieve better patient compliance. One such approach is “Mouth Dissolving Tablet”2-5

The concept of Mouth Dissolving Drug Delivery System emerged from the desire to provide patient with conventional mean of taking their medication. Difficulty in swallowing (Dysphasia) is a common problem of all age groups, especially elderly and pediatrics, because of physiological changes associated with these groups of patients.6-7

Other categories that experience problems using conventional oral dosage forms includes are the mentally ill, uncooperative and nauseated patients, those with conditions of motion sickness, sudden episodes of allergic attack or coughing. Sometimes it may be difficult to swallow conventional products due to unavailability of water.8 These problems led to the development of novel type of solid oral dosage form called “Mouth Dissolving Tablets”. This tablet disintegrates instantaneously when placed on tongue, releasing the drug that dissolves or disperses in the saliva.8

produce rapid onset of action9 In such a cases Bioavailability of drug is significantly greater than those observed from conventional tablet dosage form.10 The dispersible tablets allows dissolution or dispersion in water prior to administration but the Mouth Dissolving Tablet instead of dissolving or disintegrating in water is expected to dissolve

2. Definition
United States Food and drug administration (FDA) defined fast dissolving tablet (FDT) as “a solid dosage form containing medicinal substance or active ingredient which disintegrate rapidly usually within a matter of seconds when placed upon the tongue”11 Fast dissolving tablets are also known as mouth-dissolving tablets, melt-in mouth tablets, Orodispersible tablets, rapidmelts, porous tablets, quick dissolving tablet. Fast dissolving tablets dissolve or disintegrate In the oral cavity without the need of water.

3. Characteristics of fast dissolving tablets12
Convenient and easy to administer as does not require water for oral administration

➢ Durable and sufficient strength to withstand the rigors of the manufacturing process and manufacturing handling
➢ Pleasant mouth feel.
Insensitive to environmental conditions such as humidity and temperature.
Adaptable and amenable to existing processing and packaging machinery
Cost effective
Compatible with taste masking

4. Salient features of mouth dissolving drug delivery system

- Ease of administration to patients who refuse to swallow a tablet, such as pediatric and geriatric patients and psychiatric patients.
- Convenience of administration and accurate dosing as compared to liquids.
- No need of water to swallow the dosage from, which is highly convenient feature for patients who are traveling and do not have immediate access to water.
- Good mouth feel property of Mouth dissolving drug delivery system helps to change the basic view of medication as "bitter pill", particularly for pediatric patients.
- Rapid dissolution and absorption of drug, which may produce rapid onset of action.
- Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach, and in such cases bioavailability of drug is increased. Disintegrate in 10-20 sec. Even solvents like cyclohexane, benzene can be used as pore forming agents.

5. Benefits of mouth dissolving tablets

- Ease of Administration to the patient who cannot swallow, such as the elderly, stroke victims, bedridden patients, patient affected by renal failure and patient who refuse to swallow such as pediatric, geriatric & psychiatric patients.
- No need of water to swallow the dosage form, which is highly convenient feature for patients who are traveling and do not have immediate access to water.
- Rapid dissolution and absorption of the drug, which will produce quick onset of action.
- Some drugs are absorbed from the mouth, pharynx and esophagus as the saliva passes down into the stomach. In such cases bioavailability of drug is increased.
- Pregastric absorption can result in improved bioavailability and as a result of reduced dosage; improve clinical performance through a reduction of unwanted effects.
- Good mouth feel property helps to change the perception of medication as bitter pill particularly in pediatric patient.
- The risk of chocking or suffocation during oral administration of conventional formulation due to physical obstruction is avoided, thus providing improved safety.
- Beneficial in cases such as motion sickness, sudden episodes of allergic attack or coughing, where an ultra rapid onset of action required.
- An increased bioavailability, particularly in cases of insoluble and hydrophobic drugs, due to rapid disintegration and dissolution of these tablets.
- Stability for longer duration of time, since the drug remains in solid dosage form till it is consumed. So, it combines advantage of solid dosage form in terms of stability and liquid dosage form in terms of bioavailability.
- New business opportunity like product differentiation, product promotion, patent extensions and life cycle management.

6. Formulation Aspect for FDT

6.1 Superdisintegrants: As FDT require faster disintegration. So, pharmacist needs to formulate disintegrants i.e. superdisintegrants which are effective at low concentration and have greater disintegrating efficiency and they are more effective intragranularly. But have one drawback that it is hygroscopic therefore not used with moisture sensitive drugs. And this superdisintegrants act by swelling and due to swelling pressure exerted in the outer direction or radial direction, it causes tablet to burst or the accelerated absorption of water leading to an enormous increase in the volume of granules to promote disintegration.

Figure 1. Mechanism of superdisintegrants by swelling
6.2 Taste-masking agents: Taste masking of drug may be achieved with preventing the exposure of drug to the tongue through processing or adding competing taste-masking agents. Exposure of solubilized drug to the oral cavity can be prevented by encapsulation in polymer systems or complexation. The approaches are as follows:
- Layering the drug onto inert beads using a binder followed by coating with a taste-masking polymer.
- Granulating the drug and coating with a taste masking polymer.
- Spray drying the drug dispersed or dissolved in a polymeric solution to get taste-masked particles.
- Complexation by the use of inclusion in cyclodextrins.
- Psychological modulation of bitterness.
- Coacervation to form microencapsulated drug within a polymer.
- Formation of pellets by extrusion spheronization

6.3 Sweeteners
Sucrose and other natural sweeteners, such as Sorbitol, can be used in effervescent products, although artificial sweetening agents are customary. However, the application of artificial sweeteners is restricted by health regulations. Therefore, the use of such sweeteners will vary from one country to the next based on national standards. Saccharin or its sodium and calcium salts are used as sweeteners. Aspartame is also employed as a sweetener in effervescent tablets. Earlier, cyclamates and cyclamnic acid were the artificial sweeteners of choice, but their use has now been restricted. Some commonly used sweeteners are
- Sorbitol
- Mannitol
- Hydrogenated starch hydrolysate
- Maltitol solution
- Maltitol
- Xylitol
- Erythritol
- Glycerin
- Sucrose
- Fructose
- Maltose

7. Approaches to FDT Development
The basic approaches to develop rapidly dissolving oral dosage forms include maximizing the porous structure of the tablet matrix, incorporating the appropriate disintegrating agent and using highly water soluble excipients in the formulation. Industry observers point to broadening uses of ODT technology. These include the incorporation of macromolecules. The success for other products will depend on bioavailability requirements and the application of methods to overcome oral absorption barriers. Other areas include: the incorporation of encapsulated APIs to achieve modified-release profiles within the convenience of an FDT; and the further development of superdisintegrants for incorporation into conventional, compressed tablets, potentially widening the opportunity for ODT development. Although several technologies are available, few have reached commercial marketed products. Several methods are employed in the preparation of oral fast-dispersing tablets. The choice of material(s) depends on their rapid dissolution in water, sweet taste, low viscosity to provide ‘smooth melt feeling’, and compressibility. Even though the various formulations share some commonalities in terms of excipients selection, there is a distinct preparation method for each technology.

Conventional Techniques for preparing Fast Dissolving Tablets
1. Sublimation
2. Moulding
3. Freeze Drying
4. Spray-Drying
5. Melt-Extrusion
6. Direct Compression
7. Cotton candy process
8. Compaction
9. Nanonization
10. Three dimensional Printing(3DP)
11. Microwave Radiation
12. Fast-melting tablets based on highly plastic granules
13. Phase transition method (PTM)

7.1 Sublimation technique
Conventional tablets with high water soluble ingredients fail to disintegrate rapidly because of their low porosity and this suggests that the presence of a highly porous particle structure in the tablet matrix is an important factor for fast disintegration of FDT. In the sublimation process, volatile substances like camphor, ammonium carbonate, ammonium bicitartrate, benzoic acid, hexamethonium tetramine, naphthalene, phthalic anhydride, urea and urethane were used along with other excipients.
Solvents such as cyclohexane/benzene were sometimes also used for further enhancement in the porous matrix formation. Volatilization of these materials eliminates the complicated process associated with the lyophilization process, that is, sublimation of frozen water. The volatile materials include urea, ammonium carbonate, ammonium bicarbonate, hexa methylene tetramine, and camphor. To generate a porous matrix, volatile ingredients are incorporated in the formulation that is later subjected to a process of sublimation. Highly volatile ingredients like ammonium bicarbonate, ammonium carbonate, benzoic acid, camphor, naphthalene, urea, urethane and phthalic anhydride may be compressed along with other excipients into a tablet. This volatile material is then removed by sublimation leaving behind a highly porous matrix. Tablets manufactured by this technique have reported to usually disintegrate in 10-20 sec. Even solvents like cyclohexane, benzene can be used as pore forming agents.

**Figure 2. Mechanism of Sublimation technique**

![Diagram](image)

### 7.2 Moulding

The tablets manufactured in this manner are less compact than the compressed tablets and posses a porous structure that hastens dissolution. However, molded tablets typically do not have great mechanical strength. 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. The taste masked drug particles were prepared by spray congealing, a molten mixture of hydrogenated cottonseed oil, sodium carbonate, lecithin, polyethylene glycol, and an active ingredient, into a lactose based tablet triturate form. Compared to the lyophilization technique, tablets produced by the molding technique are easier to scale up for industrial manufacture. Moulding process includes moistening, dissolving, or dispersing the drug with a solvent then moulding the moist mixture into tablets (compression moulding with lower pressure than conventional tablet compression), evaporating the solvent from drug solution, or suspension at ambient pressure (no vacuum lyophilisation), respectively. The moulded tablets formed by compression employed are lower than conventional tablets, the moulded tablet results in highly porous structure, which increases the disintegration and dissolution rate of the product. However, to further improve dissolution rate of the product powder mixture should be sieved through very fine screen. As moulding process is employed usually with soluble ingredients (saccharides) which offers improved mouth feel and disintegration of tablets. However, moulded tablets have low mechanical strength, which results in erosion and breakage during handling.

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

**a.) Compression moulding**

This manufacturing process involves moistening the powder blend with a hydroalcoholic solvent followed by pressing into mould plates to form a wetted mass (compression moulding). The solvent is then removed by air drying, a process similar to the manufacture of tablet triturates. Such tablets are less compact than compressed tablets and possess a porous structure that hastens dissolution.

**b) Heat-Moulding Process**

Heat-moulding process involves setting the molten mass containing a dispersed drug. This process uses agar solution as a binder and a blister packaging well as a mould to manufacture the tablet. A suspension containing drug, agar and sugar is prepared followed by pouring the suspension into the blister packaging well, solidifying the agar solution at room temperature to form a jelly and finally drying at approximately 30 °C under vacuum.

**c). Vacuum Evaporation**

This process involves pouring of the drug excipient mixture (in the form of a slurry or paste) into a mould of desired dimension, freezing the mixture to form a solidified matrix and finally subjecting it to vacuum drying at a temperature within the range of its collapse temperature and equilibrium freezing
temperature. This results in the formation of a partially collapsed matrix. This method differs from the lyophilization technique, as in the former the evaporation of free unbound solvent occurs from a solid through the liquid phase to a gas, under controlled conditions, instead of the sublimation which takes place in the latter process. Unlike lyophilization, vacuum drying helps to densify the matrix and thereby improves the mechanical strength of the product. Pebley et al. evaporated the frozen mixture containing a gum (e.g., acacia, carrageenan, guar, tragacanth or xanthan), a carbohydrate (e.g., dextrose, lactose, maltose, mannitol or maltodextrin) and solvent in a tablet-shaped mould to design a MDT with a disintegration time of about 20–60 secs.

7.3 Freeze Drying/lyophilization technique

The freeze-drying technique has demonstrated improved absorption and increase in bioavailability. 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. A typical procedure involved in the manufacturing of mouth 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 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.

**Figure 3 Principle of the lyophilization technique**

The principle of the lyophilization technique is drying carried out at low temperature under conditions involving removal of water by sublimation. In this technique the material is initially frozen below \(-18^\circ\)C and then reducing the pressure of the system and giving the necessary heat allows the sublimation process. This technique is extremely useful for heat sensitive drugs and biological. Here the drug is physically entrapped in a water soluble matrix, which is then freeze-dried to give a product that is highly porous and has a large surface area. Due to the porous nature of the product, the liquid medium penetrates into the interior surface of the tablet thereby enhancing its disintegration. The tablets prepared by lyophillization disintegrate rapidly in less than 5 sec. due to quick penetration of saliva in pores when placed in the oral cavity. The lyophilization process gives a glassy amorphous structure to the bulking agent and sometimes to the drug.

7.4 Spray-Drying

Spray drying can produce highly porous and fine powders that dissolve rapidly. The formulations are incorporated by hydrolyzed and non hydrolyzed gelatins as supporting agents, mannitol as bulking agent, sodium starch glycolate or crosscarmellose sodium as disintegrating and an acidic material (e.g. citric acid) and / or alkali material (e.g. sodium bicarbonate) to enhance disintegration and dissolution. Tablet compressed from the spray dried powder disintegrated within 20 seconds when immersed in an aqueous medium. Spray dryers are widely used in pharmaceuticals and biochemical processes. Due to processing solvent is evaporated rapidly; spray drying can produce highly porous, fine powder. Spray drying can be used to prepare rapidly disintegrating tablets. This technique is based on a particulate support matrix, which is prepared by spray drying an aqueous composition containing support matrix and other components to form a highly porous and fine powder. This is then mixed with active ingredients and compressed into tablets, used a spray drying technique to prepare fast dissolving tablets. The tablets made from this technology are claimed to disintegrate within 20 seconds.
7.5 Hot-Melt extrusion method: The drug/carrier mix is typically processed with a twin-screw extruder. The drug/carrier mix is simultaneously melted, homogenized and then extruded and shaped as tablets, granules, pellets, sheets, sticks or powder. The intermediates can then be further processed into conventional tablets. An important advantage of the hot melt extrusion method is that the drug/carrier mix is only subjected to an elevated temperature for about 1 min, which enables drugs that are somewhat thermolabile to be processed. It is composed of active ingredient and carrier, and prepared by hot-stage extrusion using a co-rotating twin-screw extruder. The concentration of drug in the dispersions is always 40% (w/w). The screw-configuration consists of two mixing zones and three transport zones distributed over the entire barrel length, the feeding rate is fixed at 1 kg/h and the screw rate is set at 300 rpm. The five temperature zones are set at 100, 130, 170, 180, and 185°C from feeder to die. The extrudates are collected after cooling at ambient temperature on a conveyor belt. Samples are milled for 1 min with a laboratory-cutting mill and sieved to exclude particles >355µm. Melt extrusion technology includes softening of the blend using the solvent mixture of water-soluble polyethylene glycol, using methanol and passing of softened mass through the extruder machine or syringe to get a the product into a cylindrical segments using heated blade to form tablets.

7.6 Direct Compression: Direct compression represents the simplest and most cost-effective tablet manufacturing technique. This technique can now be applied to preparation of ODT because of the availability of improved excipients especially superdisintegrants & sugar-based excipients.

(a) Superdisintegrants: In many orally disintegrating tablet technologies based on direct compression, the addition of superdisintegrants principally affects the rate of disintegration and hence the dissolution. The presence of other formulation ingredients such as water-soluble excipients and effervescent agents further hastens the process of disintegration have used microcrystalline cellulose (MCC) and low substituted hydroxypropyl cellulose (HPC) to manufacture FDT. The ratio of MCC to HPC varied from 8:2 to 9:1. Ito and Sugihara investigated use of agar powder as a disintegrant because the powder absorbs water and swells without forming gel at physiological temperature. Ethylpharm (France) has introduced a Flash-dose technology, which contains coated crystals and micro granules along with the disintegrants. In this technology, two types of granules are used; a disintegrating agent (e.g. modified cellulose- cross carmellose) which has a high swelling force, and a swelling agent (e.g. starch) which has a low swelling force.

(b) Sugar Based Excipients: This is another approach to manufacture FDT by direct compression. The use of sugar-based excipients especially bulking agents like dextrose, fructose, isomalt, lactitol, maltitol, maltose, mannitol, sorbitol, starch hydrolysate, polydextrose and xylitol, which display high aqueous solubility and sweetness, and hence impart taste masking property and a pleasing mouthfeel.

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 maltitol) exhibit high mouldability and low dissolution rate. Mouldability is defined as the capacity of the compound to be compressed/molded. The mouldability of type 1 saccharide can be improved by granulating it with type 2 saccharides. WOWTAB technology used in Benadryl fast melt tablets uses this technique. Most commercial ODTs have been developed
using mannitol as the bulk excipient of choice. Mannitol is overwhelmingly preferred over lactose because of its extremely low hygroscopicity, excellent chemical and physical compatibility, good compressibility and better sweetness. MDT formulators prefer to use a directly compressible mannitol, which enables the preparation of robust tablets that can withstand processing and transportation. Specially textured directly compressible, spray-dried, or granulated mannitol excipients have been designed to meet these needs. These excipients under defined manufacturing conditions give a highly porous structure and friable exterior structure which helps in faster disintegration of MDT, they also provide a satisfactory mouth feel and so suitable for use in preparation of harder MDT by direct compression at low pressure.

7.7 Cotton Candy Process 22: The cotton candy process is also known as the “candy floss” process and forms on the basis of the technologies such as Flash Dose (Fuisz Technology). An oral dispersible tablet 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 oral dispersible tablet. However, the high processing temperature limits the use of this technology to thermostable compounds only. The tablets manufactured by this process are highly porous in nature and offer very pleasant mouthfeel due to fast solubilization of sugars in presence of saliva. The manufacturing process can be divided into four steps as detailed below.

a.) Floss Blend 23: In this step, 80% sucrose in combination with mannitol/dextrose and 1% surfactant is blended to form the floss mix. The surfactant acts as a crystallization enhancer in maintaining the structural integrity of the floss fibers. It also helps in the conversion of amorphous sugar into crystalline form from an outer portion of amorphous sugar mass and subsequently converting the remaining portion of the mass to complete crystalline structure. This process helps to retain the dispersed drug in the matrix, thereby minimizing migration out of the mixture.

b.) Floss Processing 24: The floss formation machine uses flash heat and flash flow processes to produce matrix from the carrier material. The machine is similar to that used in ‘cotton-candy’ formation which consists of a spinning head and heating elements. In the flash heat process, the heat induces an internal flow condition of the carrier material. This is followed by its exit through the spinning head (2000–3600 rpm) that flings the floss under centrifugal force and draws into long and thin floss fibers, which are usually amorphous in nature.

c.) Floss Chopping and Conditioning 25: This step involves the conversion of fibers into smaller particles in a high shear mixergranulator. The conditioning is performed by partial crystallization through an ethanol treatment (1%) which is sprayed onto the floss and subsequently evaporated to impart improved flow and cohesive properties to the floss.

d.) Blending and Compression 26: Finally, the chopped and conditioned floss fibers are blended with the drug along with other required excipients and compressed into tablets. In order to improve the mechanical strength of the tablets, a curing step is also carried out which involves the exposure of the dosage forms to elevated temperature and humidity conditions, (40°C and 85% RH for 15 min). This is expected to cause crystallization of the floss material those results in binding.

7.8 Compaction 27: In the compaction process, a mixture of particulate matter is fed to a compression device which promotes agglomeration due to pressure. Continuous sheets of solid material or solid forms such as briquettes or tablets are produced. Compaction processes range from confined compression devices such as tableting to continuous devices such as roll presses, Briqueting machines and extrusion. The following different techniques are based on the compaction mechanism.

a. Crystalline transition process: FDTs are prepared by crystalline transition through compressing two saccharides having high and low compressibility/moldability indices and are then subjected to the conditioning process. Transition from the amorphous
to crystalline state is intentionally done by the conditioning process after tablet compression to achieve sufficient hardness and fast disintegration time. Fluidized bed granulator is commonly used for the crystalline transition process. Particle modification can be carried out by coating or granulating a low compressible saccharide with high compressible saccharides. Mizumoto et al. studied the properties of the tablets prepared using the combination of low and high compressible saccharide. Mannitol was used as a low compressible saccharide and maltose as a high compressible saccharide and binder for granulation. Recrystallization of maltose was done by conditioning the tablet containing amorphous maltose at 25 °C and 70 % RH. The amorphous maltose present on the surface of mannitol particles absorbs moisture during the conditioning process. When crystallization of maltose occurs, particles adhere to each other firmly, which results in increasing the tablet hardness. The disintegration time and tablet hardness were found to be 10-15 s and 4.0-5.8 kg cm⁻², respectively. The authors recommended sucrose, lactose, glucose, xylitol, mannitol, erythritol as low compressible saccharides and maltose, sorbitol, trehalose and multitol as high-compressibility saccharides in increasing order of their compressibility.

b.) Phase-transition process: It is concluded that a combination of low and high melting point sugar alcohols, as well as a phase transition in the manufacturing process, are important for making FDTs without any special apparatus. FDT were produced by compressing powder containing erythritol (melting point: 122 °C) and xylitol (melting point: 93 95 °C), and then heating at about 93 °C for 15 min. After heating, the median pore size of the tablets was increased and tablet hardness was also increased. The increase of tablet hardness with heating and storage did not depend on the crystal state of the lower melting point sugar alcohol.

7.9 Three-dimensional Printing (3DP):
Three Dimensional Printing is a novel technique used in the fabrication of complex oral dosage delivery pharmaceuticals. It is possible to engineer devices with complicated internal geometries, varying densities and diffusivities, and multiple actives and excipients. The controlled delivery of an exact dosage of a drug is frequently key to its efficacy for the patient. Controlled release of oral dosage forms, specifically tablets, is often acquired with the help of coatings semi-permeable membranes, and capsuling. The thickness coatings can be made to regulate the rate of water imbibitions into the tablet and subsequently the drug diffusion out of the tablet. One potential concern with coated tablets, however, is the tendency to rupture due to swelling or handling causing catastrophic failure and release of contents prematurely. Three Dimensional Printing (3DP) is a solid freeform fabrication (SFF) technique which employs powder processing in the construction of parts in a layer-wise manner 3DP, like other SFF methods, is capable of fabricating a part directly from a CAD model, and can handle complex features such as internal walls, tortuous channels, porosity gradients, and multiple material regions. Such features are envisioned to be used to better control drug release and obtain complex release patterns.

Based on computer-aided models, three-dimensional printing (3DP) technology can exercise local control over the material composition, microstructure, and surface texture during it layer-by-layer manufacturing process to endow the products with special properties. It can be a useful tool in the development of novel solid dosage forms.

Method: In this study, a novel fast disintegrating tablet (FDT) with loose powders in it was designed and fabricated using 3DP process. The inner powder regions were formed automatically by depositing the binder solutions onto selected regions during the layer-printing processes. Results: Environmental scanning electron microscope images clearly showed that the printed regions were bound together. The particle size was reduced or individual particles could no longer be distinguished. In contrast, the unprinted regions were uncompacted with cracks and fissures among the loose powders. The tablets had a hardness value of 54.5 N/cm(2) and 0.92% mass loss during the friability tests. The disintegration time of the tablets was 21.8 seconds and the wetting time was 51.7 seconds. The in vitro dissolution tests showed that 97.7% acetaminophen was released in the initial 2 min. Conclusion: 3DP process is able to offer novel methods for preparing FDTs.
A major challenge in the development of orally disintegrating tablets (ODTs) is to achieve a good balance between tablet hardness and disintegration time. In this study, an advanced method was demonstrated to improve these opposing properties in a molded tablet using a one-step procedure that exploits the swelling induced by microwave treatment. Wet molded tablets consisting of the delta form of mannitol and silicon dioxide were prepared and microwave-heated to generate water vapor inside the tablets. This induced either swelling or shrinking of tablets, in the extent of each being dependent on tablet formulation and manufacturing conditions. A two-level full factorial design method was used to evaluate the effects of several variables in formulation and manufacturing conditions on the tablet properties, hardness, disintegration time and change in shape. The variables investigated in this study were: ratio of silicon dioxide in formulation, water volume added in granulation, ratio of water absorbed by silicon dioxide prior to granulation, and microwave irradiation time.

Swelling of tablet by microwave irradiation was observed in the batches with high ratio of silicon dioxide and low levels of water volume. The disintegration time was clearly shortened by induction of the swelling, while tablet hardness increased. We demonstrated that the water vapor generated by microwave irradiation promoted a change in the crystalline form of mannitol from delta to beta, and that this may have contributed to an increase in tablet hardness. Additionally, it was found that new solid bridges were formed between the granules in the tablet via the pathway from dissolution of mannitol in water vapor to congelation, resulting in an increase in tablet hardness. Thus, both tablet hardness and disintegration properties of the molded tablets were improved by the proposed one-step method and the appropriate ranges for variables are indicated. In addition, multiple regression modeling was used to optimize formulation and manufacturing conditions, and the tablets obtained under these optimized conditions showed both swelling and desirable tablet properties. Therefore, we concluded that this one-step method using microwave irradiation would be a useful method for preparing the ODTs.

Microwave technology has been widely used in food processing for the purpose of heating, thawing, sterilizing and bulking. Some applications for pharmaceutical processing have also been reported. For example, a solid dispersion was prepared from physical mixture containing ibuprofen, PVP/VA 60/40 and beta-cyclodextrin by microwave radiation treatment.

The concept proposed here utilizes microwave radiation (Fig. 7); we hypothesized that it could produce water vapor from the water carrier in a wet molded tablet and could also dissolve the surface of sugar alcohol granules to form new solid bridges between particles. Water vapor can also expand the pores inside molded tablets creating new channels for water uptake without the need for sublimation and/or chemical reaction that generates gas like carbon dioxide. Therefore, we predicted that the new solid bridges between particles would increase tablet hardness and the new channel for water uptake would contribute to shorten the disintegration time.
7.11 Fast-melting tablets based on highly plastic granules

Highly plastic granules that can be compressed into tablets at low pressure were developed to make fast-melting tablets (FMTs) by compression method. The highly plastic granules are composed of three components: a plastic material, a material enhancing water penetration, and a wet binder. One of the unique properties of the highly plastic granules is that they maintain a porous structure even after compression into tablets. The porous and plastic nature of the granules allows fast absorption of water into the compressed tablet for fast melting/dissolution of the tablet. The prepared tablets possess tablet strength and friability that are suitable for multi-tablet packages. The three-component highly plastic granules provide an effective way of making FMTs by compression.

Figure. 8 A general processing step for making highly plastic granules and fast dissolving tablet

7.12 Nanonization

Nanonization is a quite new technique to development of FDT using nanocrystal formulations in order to optimise dissolution properties of lipophilic, poorly soluble drug piroxicam (PRX). Different nanocrystal formulations were prepared using a high pressure homogenisation technique and poloxamer 188 as stabiliser. Characterisation of PRX nanocrystal FDT was carried out by infrared spectroscopy (FTIR), X-ray powder diffractometry (XRPD), differential scanning calorimetry and photon correlation spectroscopy. Dissolution study of PRX FDT was performed in distilled water (pH 5.5) and was compared to that of PRX coarse suspension FDT, PRX/poloxamer 188 physical mixture and bulk PRX samples. The XRPD and FTIR studies demonstrated that the homogenisation process led to a polymorphic transition from form I (bulk commercial PRX) to form III and monohydrate form of the nanocrystals. All ODT formulations prepared using PRX nanosuspensions showed a higher PRX dissolution rate compared with the FDT prepared with the coarse PRX. Since the solubility of the different PRX polymorphic forms increased only slightly from bulk PRX (form I) to monohydrate, form II and form III, we can conclude that the improvement in PRX dissolution rate is mainly caused by the increased surface-to-volume ratio due to the submicron dimension of the drug particles.

Figure 9 Illustration of FDT by Nanonization

7.13 Phase transition method (PTM)

Saccharides and sugar alcohols can be categorized not only by compressibility but also by melting point. Based on the melting points they were divided into two groups and investigated using conventional granulation and compression apparatus. 31 Erythritol is the high melting (122°C) and xylitol the low melting (93°C) sugar alcohol. Erythritol and xylitol were used as a diluent and a binder, respectively for fluid bed granulation. After compression, the resulting tablets were placed in a drying oven and heated at a temperature close to the melting point of xylitol (approximately 93°C). Conditions were maintained for a certain period of time and the tablets then allowed to cool to room temperature. The hardness of the processed tablets was found to increase with increasing xylitol content. Xylitol melted, diffused, and solidified again in the heated tablets resulting in a greater bonding surface area between the powder particles and increased hardness. Tablets containing about 5% xylitol showed hardness of 4 kp and an oral disintegration time of < 30 s.
8. Patented technologies for preparing Fast Dissolving Tablets

1. Zydis technology
2. Takeda technology
3. Novartis technology
4. Nippon Shinyaku technology
5. Flashtab technology
6. Wowtab technology
7. Daiichi technology
8. Orasolv technology
9. Ziplets technology
10. Lyoc technology
11. Nanocrystal technology
12. Pharmabrust technology
13. Advantol technology
14. Frosta technology

8.1 Zydis® technology: Freeze drying is a process in which solvent is removed from a frozen drug solution or a suspension contains structure–forming excipients. The resulting tablets are usually very light and have a highly porous structure that allows rapid dissolution or disintegration. When placed on the tongue, the freeze-dried unit dissolves almost instantly to release the incorporated drug. The entire freeze drying process is done at non elevated temperature to eliminate adverse thermal effects that may affect drug stability during processing. When stored in a dried state, the freeze-dried dosage form has relatively few stability problems during its shelf life. The freeze-drying process may result in a glassy amorphous structure of excipients as well as the drug substance, leading to the enhanced dissolution rate. Leading to the enhanced Tablet is produced by lyophilizing or freeze-drying the drug in a water-soluble matrix material, usually consisting of gelatin. Freeze-drying is done in blisters, where sublimation removes water, which are then sealed and further packed. The resultant product is very porous, light, fragile and disintegrates immediately on contact with saliva. The Zydis® formulation is also self-preserving since the final water concentration in the freeze-dried product is very low and prevents microbial growth. The ideal drug candidates for Zydis® are those which one showing relatively low water solubility, with fine particles and good aqueous stability in the suspension. For water-soluble drugs, the upper limit for drug loading is very low (approx. 60 mg).

Zydis® (R.P. Scherer, Swindon, UK), using freeze drying processes, is one of the first generations of fast disintegrating dosage forms. There are approximately 12 marketed Zydis® products, including lorazepam, piroxicam, loperamide, loratidine, enalapril and selegiline. These formulations are freeze-dried products of a combination of water-soluble matrix material with drug, which is preformed in blister pockets and freeze dried to remove the water by sublimation. The resultant structures are very porous in nature and rapidly disintegrate or dissolve upon contact with saliva. The process had undergone several modifications to accommodate drugs with different physicochemical characteristics, drug loading and particle size, and matrix modifications to result in an acceptable dosage form. Drug loading for water insoluble drugs approaches 400 mg. The ideal drug characteristics are relative water insolubility with fine particle size and good aqueous stability in the suspension. As the dose is increased, it becomes more difficult to achieve the optimum formulation. The formulation can also contain taste-masking agents such as sweeteners, flavorings, pH-adjusting substances such as citric acid, and preservatives such as parabens to ensure aqueous drug suspension stability prior to the freeze-drying step. Finally, the freeze-dried formulations are manufactured and packaged in PVC or PVDC plastic packs, or may be packed into Aclar laminates or aluminum foil–foil preparations to protect the product from external moisture.

8.2 Takeda® technology: The wetted mass was compressed at low pressure and...
subsequently dried to produce porous tablets with sufficient mechanical strength. The disintegration time was about 30–50 seconds in the mouth. In a patent by Novartis Consumer Health (Basel, Switzerland), the drug solution or suspension was dispersed into molds. The solvent was removed from the units usually by heating, pressure reduction, or microwave radiation. In a patent by Takeda\(^4\), the molded tablets contained a drug, a saccharide having a solubility of 30 (w/w)% or less at room temperature (e.g., lactose and mannitol), and a saccharide having a solubility of 30 (w/w)% or more at room temperature (e.g., glucose, fructose, sucrose, xylose, trehalose, xylitol, sorbitol, erythritol, dextrin, and pullulan). The amount of this saccharide was slightly above its solubility. The mixture was a creamy aqueous suspension having both low solubility and high solubility saccharides in water. The moisture was then removed from the suspension to obtain molded tablets. Pebley et al. described a vacuum drying process. The matrix network of the tablet included a gum, a carbohydrate, and the drug. Vacuum drying of the tablet above its collapse temperature instead of freeze drying below its collapse temperature provides a process for producing tablets with enhanced structural integrity, while rapidly disintegrating in normal amounts of saliva.

8.3 FlashTab technology: FlashTab\(^5\) technology (Ethypharm, France) produces tablets by compression of granular excipients. This technology uses almost the same excipients as do conventional compressed tablets. While rapidly disintegrating in normal amounts In this technique most of the excipients are used in combination with coated drug particles to produce a tablet that disintegrates in the mouth in one minute. FlashTab matrix tablet contains a swelling agent such as modified starch or microcrystalline cellulose and superdisintegrant such as rospovidone or croscarmellose. The system may also contain a highly water soluble polol such as mannitol, Sorbitol, maltitol or xylitol with binding properties if no swelling agents is used. The direct coating procedure used for taste making of the active ingredients. In the FlashTab technique the excipients are first granulated using wet or dry granulation. Then they are mixed with coated drug particles and compressed into tablets using conventional processing equipment. Tablets containing hygroscopic materials can be also blister packed using high quality polyvinyl chloride (PVC) or aluminum foils. These packing materials provide a higher degree of moisture protection than normal PVC foils. Excipients used in this technology comprise two groups of components: disintegrating agents such as carboxymethylcellulose or insoluble reticulated polyvinylpyrrolidone and swelling agents such as starch, modified starch, carboxymethylated starch, microcrystalline cellulose, and possibly directly compressible sugars. The mixture of excipients is prepared by either dry or wet granulation methods.

8.4 WowTab\(^5\): WowTab technology was developed by Yamanouchi Pharma Technologies, USA. WowTab tablets have sufficient hardness to maintain the physical characteristics of the dosage form during the production and distribution. WowTab\(^5\) technique utilizes saccharides because they possess the properties of fast dissolution in water or saliva and achieve the required tablet hardness upon compaction. However, no single individual saccharide possesses both these properties. They either possess fast disintegration properties or good hardness upon compaction. For example, maltitol, lactose, glucose, sucrose and erythritol showed very quick dissolution characteristics and low compressibility and were called low moldable sugars. Maltose, sorbitol, trehalose and maltitol were called high moldable sugars as they show adequate hardness upon compression, good binding and slow in vivo disintegration time. The term moldability is defined as the capacity of the compound to compress and dissolve rather than formation of a true molding by solvent wetting and melting. A new formulation composition was generated by granulation of a low moldable sugar with a high moldable sugar. The tablet prepared by compression of the above composition, exhibited both fast disintegration and adequate hardness characteristics after humidification and drying. The resulting tablet had a hardness of at least 1.0-2.0 kg and disintegration time of 1-40s. The taste masking technique utilized in WowTab\(^5\) is proprietary but it offers superior mouth feel due to smooth melt action.

8.5 OraSolv\(^5\): OraSolv technology (Cima Labs) produced tablets by low compression pressure. It uses and effervescient disintegration pair that releases gas upon contact with water. The used effervescent disintegration pair that
releases gas upon contact with water. Orasolv® technology can accommodate a wide range of APIs from less than 1 mg to as high as 500 mg. The effervescent mixture comprises two dry ingredients: an effervescent acid (malic acid, tartaric acid, citric acid) and an effervescent base (sodium carbonate, potassium carbonate, potassium bicarbonate). They undergo an effervescent reaction when they come in contact with aqueous solutions resulting in the generation of CO2. The widely used effervescent disintegration pairs usually include an acid source and a carbonate source. The acid source include citric acid, malic acid, fumaric acid, adipic acid and succinic acids. The carbonate sources include sodium bicarbonate, sodium carbonate. The carbon dioxide evolved from the reaction may provide some “fizzing” sensation, which is a positive organoleptic sensation. The amount of effervescent agent is in general about 20-25% of the total tablet. Because of the soft and fragile nature of OraSolv tablets a special packaging system known as PakSolv®, was developed to protect the tablets from breaking during transport and storage. PakSolv® is a dome-shaped blister package that prevent the vertical movement of the tablet within the depressions, because the diameter of the lower portion of the dome is too narrow to accommodate the tablet. PakSolv® also offer light, moisture and child resistance.

**8.6 Durasolv®.**

Durasolv® is Cima’s second-generation orally disintegrating tablet formulation manufactured in a similar fashion to Orasolv®, but the tablets produced contain non-directly compressible fillers (sugars and SAs, such as dextrose, mannitol, sorbitol, lactose and sucrose) and a lubricant. The ingredients are fine particles that provide a large surface area for improving the dissolution rate. Disintegrants are avoided in the formulation but wicking agents such as carbopol, gums (gum arabic and xanthan), and hydroxyl alkyl celluloses (hydroxyl ethyl cellulose and hydroxyl propyl methyl cellulose) are added to assist water entry into the tablet. Durasolv® has much higher mechanical strength than Orasolv® due to the use of higher compaction pressure during tableting and hence the product can be packed in either traditional blister packs or vials. The newest Durasolv® formulation, NuLev®, is actually dispensed in stock bottles. However, care must be taken as the time of dispensing tablets from stock bottles because excess exposure to high RH conditions may introduce enough moisture to initiate dissolution of the tablet matrix. The advantage of this technique includes its low cost of production, faster production rate, standard manufacturing technique, standard material, packaging format and low cost and risk dependence. A disadvantage of Durasolv® is that the technique is not applicable for a large dosage of APIs. As the formulation is subjected to high pressure during the compaction process, the bitter taste of the drug is exposed to the patient’s taste buds and therefore Durasolv® technology is suitable for formulation of small dose tablets of APIs. Other disadvantage is that Durasolv® has a slightly longer disintegration time.

**8.7 Ziplets® technology**

Recently, the Ziplet technology was developed, which can be used for water insoluble drugs or drugs as coated microparticles. It was found that the addition of a suitable amount of a water-insoluble inorganic excipient combined with one or more effective disintegrants imparted an excellent physical resistance to the MDT and simultaneously maintained optimal disintegration even at low compression force and tablet hardness. In fact, breakage of the tablet edges or formation of powder during manufacturing and opening of the blister pack is avoided because of its superior mechanical resistance. The use of water-insoluble inorganic excipients also offers better enhancement of disintegration characteristics in comparison to the most commonly used water-soluble sugars or salts. In fact, tablets composed primarily of water-soluble components often tend to dissolve rather than disintegrate, resulting in much longer disintegration time. As the soluble components dissolve on the tablet’s outer layer, a concentrated viscous solution is formed, which reduces the rate of water diffusion into the tablet core.

**8.8 Takeda® (Osaka, Japan)**

Takeda® has developed compression-moulded mixtures containing a drug and a combination of starches and sugars with...
surfaces that have been wetted with a suitable amount of water. The wetted mass is compression moulded and dried and porous tablets (with sufficient mechanical strength to resist destruction during further manufacturing) are obtained. The FMT, the weight of which can reach 1–2 g, has a sufficiently rapid disintegration time in the mouth (30–50 s according to examples reported.

8.9 Lyoc technology®
In the Lyoc® formulation, the porous solid form is obtained by freeze drying an oil-in-water emulsion placed directly in the blister pockets. In order to prevent in homogeneity by sedimentation during freeze drying this formulation requires a large proportion of un-dissolved inert filler to increase the viscosity of the suspension. The high proportion of filler reduces the porosity of the tablet, and as a result, the disintegration is slower. It is also noted that the tablet still has poor mechanical resistance. The high proportion of filler reduces the potential porosity of the dried dosage form and results in denser tablets with disintegration rates that are comparable with the loosely compressed fast melt formulations.

8.10 Pharmaburst®
Pharmaburst® is an engineered co-processed excipients system, which is used as a quick disintegrating matrix in the manufacture of ODT using standard manufacturing equipment and packaging lines. ODTs are generally manufactured by dedicated companies that have specialized manufacturing and packaging equipment because of the complexities of the dosage form, such as low tablet hardness and high friability. Naturally, high costs and fees are then associated with this approach. Pharmaburst allows the customer to keep control of the formulation development process because its ODT products can be developed in the customers’ facility with standard tablet presses and tooling. The resultant tablets are very robust with low friability and fast disintegration, allowing packaging into blisters or bottles using standard packaging equipment.

8.11 Frosta® technology
The initial success of the FDT formulation led to the development of various technologies. These technologies, however, still have some limitations. Recently, a new technology called Frosta® (Akina) was developed for making FDTs. The Frosta® technology utilises the conventional wet granulation process and tablet press for cost-effective production of tablets. The Frosta® technology is based on the compression of highly plastic granules at low pressures to prepare FDTs. The highly plastic granules are composed of three components: a plastic material, a water-penetration enhancer and a wet binder. Each of the three components plays an essential role in obtaining tablets with higher strength and faster disintegration time than the other FDTs. The Frosta® tablets are mechanically strong with friability of 1% and are stable in accelerated stability conditions when packaged into a bottle container. They are robust enough to be packaged in multi-tablet vials. Conventional rotary tablet presses can be used for the production of the tablets and no other special instruments are required. Thus, the cost of making FDTs is lower than that of other existing technologies. Depending on the size, Frosta tablets can melt in 10 sec. after placing them in the oral cavity for easy swallowing. The Frosta® technology is ideal for wide application of FDTs technology to various drug and nutritional formulations.

The key benefits of the Frosta® technology are:
• Fast disintegration in the mouth: within 5-40 sec depending on the tablet size.
• Low manufacturing cost: the same as making conventional tablets.
• Strong mechanical property: friability 1%
• Multi-tablet packaging: dozens of tablets in one bottle.

Simple processing: one-step wet granulation processing

8.12 Advantol® technology
Advantol™ is a directly compressible excipients system offering "Soft-Melt" functionality and specially formulated for nutraceutical applications. SPI Pharma’s Advantol platform uses proprietary co-processing technology. Advantol requires no special manufacturing equipment or tooling. Advantol formulations utilize a standard rotary tablet press with standard tooling under normal tableting temperature and humidity conditions to make robust “soft-melt” tablets. SPI Pharma’s Advantol® platform uses proprietary co-processing technology. It can be used to develop a "soft-chew" or a "quick-melt" solid dosage form for tablet applications. Advantol® is a robust, off-the-shelf excipient system that allows the formulator to carry out product development work in their lab giving the company control of the development and
testing activities. In addition, Advantol® requires no special manufacturing equipment or tooling. Advantol® formulations utilize a standard rotary tablet press with standard tooling under normal tableting temperature and humidity conditions to make robust "soft-melt" tablets. In contrast to using wet granulation or spray drying methods, SPI's technology allows customers to simply add the active to Advantol®, dry blend and compress, thus reducing the production cycle time and lowering costs.

8.13 NanoCrystal™

NanoCrystal™ technology (Elan, King of Prussia, Pennsylvania) uses orally administered Nanoparticles (<2 µm) in the form of rapidly disintegrating tablet matrix. The NanoCrystal™ orally disintegrating tablet dosage form was developed to facilitate the preparation of small-scale clinical supplies. NanoCrystal™ colloidal dispersions of drug substance are combined with water-soluble ingredients, filled into blisters, and lyophilized. The is approach is especially attractive when working with highly potent or hazardous materials because it avoids manufacturing operations such as granulation, blending, and tableting, which generate large quantities of aerosolized powder and present much higher risk of exposure. The freeze-drying approach also enables small quantities of drug to be converted into FDTs because manufacturing losses are negligible. The final tablet is durable enough for conventional blister or bottle packaging and accepts as much as 200 mg of drug per unit. Other features include conventional, compendial inactive components and non–moisture-sensitive inactive ingredients.

8.14 Daiichi

Daiichi (Tokyo, Japan) performed a series of experiments to develop an FMT of moderate strength, using a combination of starch or cellulose and one or more water-soluble saccharides. Erythritol was found to be the best sugar for this type of formulation, showing rapid disintegration that was negligibly affected by tablet hardness; good tolerability and sweetening; and a refreshing mouth sensation because of its endothermic dissolution heat. Tablets are produced by compressing a powder containing two sugar alcohols with high and low melting points, and subsequent heating at a temperature between the high and low melting points. Before the heating process, the tablets do not have sufficient hardness because of the low compatibility. The tablet hardness is increased after the heating process. A combination of two sugar alcohols and the heating process is needed to prepare FDT tablets with sufficient hardness. Tablet hardness is related to the increase of inter-particle bonds or the bonding surface area in tablets induced by the phase transition of the lower melting point sugar alcohol. Manufacturing of FDT tablets by the present method can be performed without any special apparatus.
### Table No. 2) List of Marketed Fast Dissolving Tablets

| S. N. | Trade Name          | Active Drug                  | Manufacturer                                      |
|-------|---------------------|------------------------------|---------------------------------------------------|
| 1.    | Abilify Discmelt    | Aripiprazole                 | Otsuka America/Bristol-Myers Squibb               |
| 2.    | Allegra ODT          | Fexofenadine                 | Sanofi Aventis                                    |
| 3.    | Aricept ODT          | Donepezil                    | Eisai Co.                                         |
| 4.    | Alavert Quick Dissolving Tablets | Loratadine | Wyeth                                              |
| 5.    | Benadryl Fastmelt   | Diphenhydramine & pseudoephedrine | Warner Lambert, NY, USA                           |
| 6.    | Claritin redi Tab    | Loratadine                   | Schering plough Corp., USA                        |
| 7.    | Cibalgina DueFast    | Ibuprofen                    | Eurand International                              |
| 8.    | Clarinex RediTabs    | Desloratadine                | Schering-Plough                                   |
| 9.    | Clonazepam ODT       | Clonazepam                   | Par Pharmaceutical                                |
| 10.   | FazaClo              | Clozapine                    | AzurPharma                                        |
| 11.   | Febrectol            | Paracetamol                  | Prographarm, Chateauneuf, France                  |
| 12.   | Felden fast melt     | Piroxicam                    | Pfizer Inc., NY, USA                              |
| 13.   | Gaster D             | Famotidine                   | Yamanouchi Pharma Tech. Inc.                      |
| 14.   | Hyoscyamine Sulfate ODT | Hyoscyamine Sulfate         | KV Pharm.Co.,Inc.                                 |
| 15.   | Klonopin Wafers      | Clonazepam                   | Roche                                             |
| 16.   | Maxalt MLT           | Rizatriptan                  | Merck and Co., NJ, USA                            |
| 17.   | Nurofen FlashTab     | Ibuprofen                    | Ethypharm                                         |
| 18.   | Olanex instab        | Olanzapine                   | Ranbaxy lab. Ltd. New-Delhi, India                |
| 19.   | Propulsid Quicksolv  | Cisapride monohydrate        | Janssen pharmaceutics                             |
| 20.   | Pepcid RPD           | Famotidine                   | Merck and Co., NJ, USA                            |
| 21.   | Relivia Flash dose   | Tramadol HCl                 | Fuisz Technology, Ltd.                            |
| 22.   | Risperdal MTab       | Risperidone                  | Janssen pharmaceutics                             |
| 23.   | Romilast             | Montelukast                  | Ranbaxy lab. Ltd. New-Delhi, India                |
| 24.   | Spasfon Lyoc         | Phloroglucinol Hydrate       | Farmalyoc                                         |
| 25.   | Torrox MT            | Rofecoxib                    | Torrent pharmaceuticals, India                    |
| 26.   | TYLENOL Meltaways     | Acetaminophen                | McNeil Consumer Healthcare                       |
| 27.   | Temptra Quicklets    | Acetaminophen                | Bristol myers Squibb, NY, USA                     |
| 28.   | Tempra Quicklets     | Paracetamol                  | Cima Labs,Inc.                                   |
| 29.   | NuLev                | Hyoscyamine Sulfate          | Cima Labs, Inc.                                   |
| 30.   | Zofran ODT           | Ondansetron                  | Glaxo Wellcome, Middlesex, UK                     |
| 31.   | Zoming-ZMT           | Zolmitriptan                 | AstraZeneca, Wilmington, USA                      |
| 32.   | Zeplar TM            | Selegiline                   | Amarin Corp., London, UK                          |
| 33.   | Zyprexia             | Olanzapine                   | Eli Lilly, Indianapolis, USA                      |
| 34.   | Zolming Repimelt     | Zolmitriptan                 | Cima Labs,Inc.                                   |

### Conclusion:

Fast-dissolve products offer improved compliance and convenience for patients. According to Technology Catalysts international (TCI), more than 200 branded and generic products have been commercialized on FDT formulations. These FDT prescription and over-the-counter products are approaching 10% of the global oral drug delivery market almost $4 billion. FDTs have potential advantages over conventional oral dosage forms with their improved patient compliance, convenience, bioavailability and rapid onset of action, which have drawn the attention of many manufactures throughout the past decade. FDT formulation obtained by some of these technologies has sufficient mechanical strength and quick disintegration/dissolution in the mouth. There is a clear opportunity for new enhanced oral products arising within this market segment. Approximately one third of the population, primarily the geriatric and pediatric populations, has swallowing difficulties, resulting in poor compliance with oral tablet which leads to reduced overall therapy effectiveness. Due to the constraints of the current FDT technologies as highlighted...
above, there is a need of improved manufacturing process for fast dissolving tablets. To fulfill these medical needs, formulators have devoted considerable effort to developing a novel type of tablets dosage form for oral administration, one that disintegrates and dissolves rapidly in saliva without the need of drinking water. The development of a fast-dissolving tablet also provides an opportunity for line extension in the marketplace; a wide range of drug can be considered candidates for this dosage form, leads to increase revenue, while also targeting underserved and under-treated patient population.

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Table 1. List of superdisintegrants used in the Fast dissolving formulations.

| Superdisintegrants | Example of | Mechanism of Action | Special Comment |
|--------------------|------------|---------------------|----------------|
| Crosscarmellose® Ac-Di-Sol® Nymce ZSX® Primellose® Solubal® Vivasol® | Crosslinked cellulose | -Swells 4-8 folds in < 10 seconds. -Swelling and wicking both. | -Swells in two dimensions. -Direct compression or granulation -Starch free |
| Crosspovidone Crosspovidon M® Kollidon® Polypsladone® | Crosslinked PVP | -Swells very little and returns to original size after compression but act by capillary action | -Water insoluble and spongy in nature so get porous tablet |
| Sodium starch glycolate Explotab® Primogel® | Crosslinked starch | -Swells 7-12 folds in <30 seconds | -Swells in three dimensions and high level serve as sustain release matrix |
| Alginic acid NF Satialgine® | Crosslinked alginic acid | -Rapid swelling in aqueous medium or wicking action | -Promote disintegration in both dry or wet granulation |
| Soy polysaccharides Emcosoy® | Natural super disintegrant | | -Does not contain any starch or sugar. Used in nutritional products. |
| Calcium silicate | | -Wicking action | -Highly porous, -light weight -optimum concentration is between 20-40% |